Conductive thiophene-based fibers synthesized by living cells as novel bioelectronic materials

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In recent years, it has been observed that living cells can be employed as active synthesis platforms for the assembly of intrinsically biocompatible bioelectronics materials. This process, which lies at the interface between living and non-living matter, is of fundamental interest since self-assembly in vivo could allow to circumvent brain-blood barrier and deliver large aggregates or even devices to the brain. Within this context, thiophene-based compounds represent workhorse materials for organic bioelectronics, owing to their biocompatibility and to the possibility to afford both electronic and ionic conduction.

Here, we report about the cell-mediated assembly of semiconductive nanofibers based on dithienothiophene-S,S-dioxide (DTTO) derivatives. Fibers originate inside cells and grow also "through" them, reaching and piercing the plasma membrane in one cell to penetrate the adjacent cell, without killing them. We extensively characterized the photophysics of DTTO molecules during the various steps of fibers production through steady state and time-resolved spectroscopy. We report the presence of DTTO aggregates inside the fibers, which represent the conductive domains of the nanostructured material and describe the interaction between DTTO molecules and the protein scaffold. By complementing the spectroscopic data with XRD characterization and electrical conductivity measurements, we discovered an extended polymorphism of DTTO in solid state. Our results suggest that the aggregation occurring in living cells is somehow unique to the biotic phase, and it involves at least part of the cell machinery. As fibers show electrical conductivity, they represent a way to directly stimulate cells or to induce artificial gap-junctions between cells, possibly affecting signal propagation as occurring in cardio-myocytes or in general to affect cell population behavior.

Further studies on the fibers' production process are in progress, with the aim to open the way to a wide range of new protein-based materials for bioelectronics and cell photostimulation.

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Dissipative charge transport in organic mixed ionic-electronic conductors.

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Charge transport in electrochemical environments is intrinsically dissipative. Electronic signals lose power and phase relation when transmitted with ionic carriers across electrolyte solutions. To overcome the problem of dissipation, nature evolved the nervous system where neurons are optimized to transmit electronic signals along axons.[1] Key mechanisms addressing dissipation include the action potential, which actively propagates the depolarization wave along the cell membrane to maintain signal amplitude and phase, and myelination, which reduces capacitive coupling to the dissipative environment.

In this work, we elaborate on the analogy between dissipative charge transport in neurons' axons and in organic mixed ionic-electronic conductors (OMIEC) to come out with a transmission line theory-based model that describes the impact of intrinsic material transport parameters on the dissipation of electronic signals. The model is confirmed with experimental transport measurements in microstructured OMIEC devices. Impedance spectroscopy, phase sensitive potential analysis and atomic force microscopy are used to directly measure signal dissipation along OMIEC channels varying channel length and doping level. Our findings deliver the dispersion relation for electronic transport in mixed conductors immersed in conductive electrolyte. To quantify dissipation in such systems we introduce the propagation constant γ as a new figure of merit for the design of OMIEC-based devices working alongside the universally recognized figure of merit μC^*.[2] In this way, we can properly account for the importance of dissipation to guide materials design and to demonstrate the feasibility of OMIEC materials for specific applications.

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Organic Electronic biosensors for health monitoring

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Bio-recognition is a fundamental mechanism in biological processes in living systems, and it is widely exploited in technological and health applications. Organic Electronics is an emerging technology perfectly suited to connect electrical and biological worlds: the biocompatibility of many materials used for the fabrication of OE devices, the ability to communicate with living systems through both ionic and electronic currents, and the high sensitivity to small variations of potential differences make OE a perfect platform for the realization of specific biosensors. Moreover, one of the main innovative features of Organic Electronics is the idea that materials properties of the components can be selectively tuned through chemical modification or designed synthetic procedures. I present recent strategies to realize biosensors based on organic transistors using as sensing elements antibodies, peptide aptamers and enzymes immobilized on one electrode surface or directly on the organic semiconductor. The works here presented will show successful biosensing strategies towards different kinds of biomarkers related to health issues, performed in model solutions as well as real samples.

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Membrane potential modulation in bacteria via push-pull azobenzene

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Optomodulation uses light to artificially alter physiological or metabolic functions in organisms on single-cell basis.[1,2] In particular we photostimulate *Bacillus subtilis* after exposure to NO_2–2(C_6-Pyr), a recently developed azobenzene molecule. Its exposure to visible light (470nm) leads to a trans-cis isomerisation reaction, accompanied by a strong change in the dipole moment thanks to the electron-donor acceptor moiety (Push-Pull effect). This in turns leads to a decrease of the membrane potential (depolarization) and a subsequent modulation of the cellular signalling.

Here, we show that a membrane-targeted azobenzene is able to modulate the membrane potential via visible light stimulation. Specifically we observed, via fluorescence microscopy, a depolarization across the cell wall that occurred within 10 seconds after a 10 seconds light pulse and the recovery of resting membrane potential lasted an amount of time dependant on the concentration of NO_2–2(C_6-Pyr). Furthermore we observed that the exposure to this molecule can also lead to an increase of the antibiotic tolerance, suggesting the involvement of membrane potential in the phenomenon.

These results show our capability to influence bacteria membrane potential with optomodulation systems, which will allow us to better understand and analyze microbial physiological mechanisms on quantitative and qualitative basis.

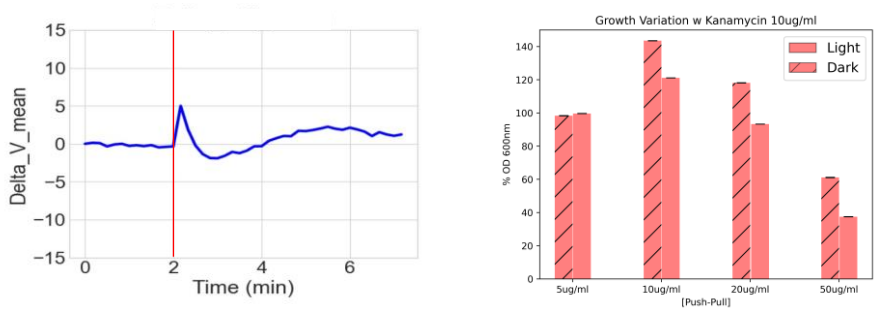

Figure 1: depolarization effect registered during the timelapse subsequent to 470nm light pulse (left) and variation of tolerance to antibiotic exposure of B. subtilis in dark condition and under light stimulation (right).

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Neuromodulation by organic semiconducting oligomers in *Hydra vulgaris*

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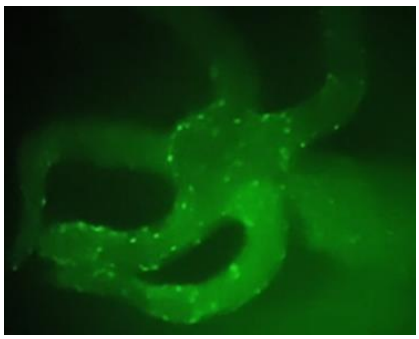
Functional materials present a promising alternative to traditional techniques for modulating neuronal function. By examining the behavioural patterns induced by neuroactive substances in simple animal models, we can gather valuable insights into their mechanisms of action and their potential for developing new therapeutic applications. The nervous system of the small freshwater polyp *Hydra*, consisting of a network of hundreds to thousands of neurons, offers a manageable yet complex framework for studying fundamental interactions between neurons and neuromodulatory compounds. This approach avoids the complications associated with more complex nervous systems. The organic semiconducting oligomer ETE-S has already been demonstrated to function as a neuromodulator in *Hydra vulgaris*, eliciting specific behavioural responses [1]. In this study, we show results from experiments in which *Hydra* was exposed to other thiophene-based trimers [2]. Using electrophysiological recordings and functional calcium imaging, we expanded our understanding of the neuromodulating effects of this class of semiconducting oligomers. These findings have the potential to illuminate fundamental chemical and physical phenomena in organic bioelectronic interfaces for neuromodulation, ultimately paving the way for innovative methods that could accelerate the development of this technology for clinical applications.



Transgenic Hydra *for calcium imaging*

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Nanoscale Investigations of Electroactuation in Organic Mixed Ionic-Electronic Conductors with Modulated-Electrochemical Atomic Force Microscopy

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Due to the combination of high ionic and electronic conductivities with soft mechanical properties, organic mixed-ionic electronic conductors (OMIECs) are a promising material platform for bioelectronic interfaces. OMIECs achieve the conversion of electrochemical processes in liquid environment to mechanical deformation and have been successfully exploited in bioelectronics soft actuators with low-voltage drive and nanoscale precision.[1] During volume change, OMIECs translate an external stimulus to a change of the physical properties on a nanometer scale, but the intrinsic mechanism of actuation is not completely understood. In this research, we face this challenge introducing the modulated electrochemical atomic force microscopy (mEC-AFM) as novel characterization method for electroactive materials. We combine frequency-resolved electroswelling measurements with electrochemical impedance spectroscopy on a mixed conductor, poly(3,4-ethylenedioxythiophene) polystyrene sulfonate (PEDOT:PSS) to correlate morphological changes with information on ionic uptake. Through multichannel mEC-AFM imaging, we obtain maps of local electroswelling amplitude and phase as well as surface morphology, revealing that both the amplitude and timescales of electroswelling are governed by the drift motion of hydrated ions (Figure 1a).[2] We explore the mEC-AFM technique to investigate microactuators based on polypyrrole doped with dodecylbenzenesulfonate (Ppy:DBS) and show how frequency dependent measurements can be exploited to achieve subsurface profiling of ion migration and swelling (Figure 1b).[3] Finally, we demonstrate how local mapping of ion uptake with mEC-AFM provides a novel method to determine the channel potential in organic electrochemical transistors (OECTs) during operation (Figure 1c).[4]

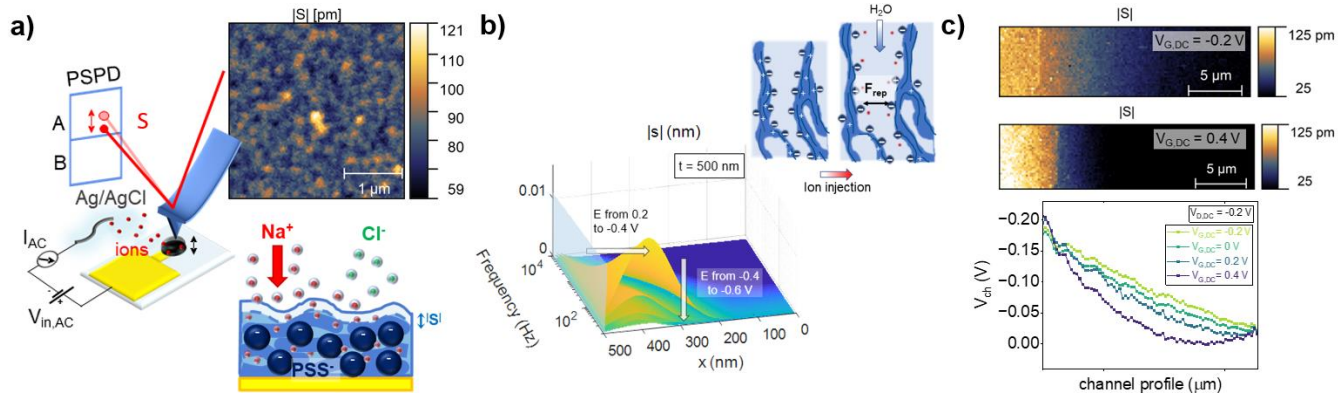

Figure 1: Nanoscale investigations of electroactuation in OMIEC materials with mEC-AFM. a) mEC-AFM microscopy of electroswelling in PEDOT:PSS. b) Spatiotemporal subsurface profile of electroswelling in a Ppy:DBS microactuator. c) In operando measurements of the local swelling and channel potential in an OECT.

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Detection of chloride in sweat with extended-gated organic electrochemical transistors

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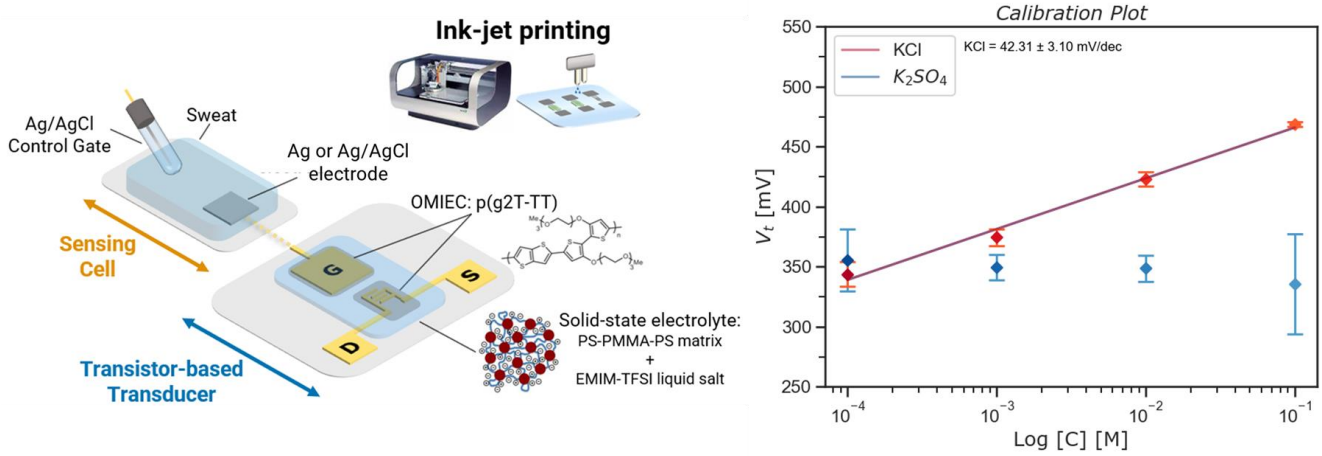
Cystic fibrosis (CF) is the most common progressive, life-limiting, multi-organ genetic disease that is caused by mutations affecting the CFTR anion channel, which is involved in chloride ion transport and fluid regulation. Diagnosis and treatment personalization are based on the monitoring of chloride levels in sweat[1]. The current clinical procedure consists of sample collection in the clinic, while the analysis is performed in a laboratory set up by experienced and trained operators. These technical and ethical limitations raise the demand for convenient sweat analysis in non-centralized healthcare facilities and personalized diagnostics[2]. Electrolyte-Gated Transistors (EGTs) have recently been shown to be a potential breakthrough in biosensing applications, since they can be effectively interfaced with biological samples transducing weak biological signal variations into readable electronic output[3]. Therefore, their high amplification gain, compatibility with cost-effective manufacturing processes, miniaturization and operation at low voltages (<1V) make them ideal candidates for low-cost point-of care or wearable devices. In this work, a printed Organic Electrochemical Transistor (OECT) based on (poly(2-(3,3-bis(2-(2-(2-methoxyethoxy)ethoxy)ethoxy)-[2,2-bithiophen]-5-yl)thieno[3,2-b]thiophene) p(g2T-TT) extended-gate comprising of a partially chlorinated silver electrode is used for the monitoring of chloride ions. This architecture allows to exploit the transduction and amplification features of OECTs to convert the potentiometric signal of the sensing element selectively and accurately[4]. The sensing element was first validated by carrying out standard potentiometry in physiologically relevant ranges of chloride, i.e. from 0.1 mM to 100 mM, obtaining a super-Nernstian sensitivity around 75 mV/dec. Additional tests employing different salts containing or not chloride were performed to assess device selectivity. Finally, the extended-gate OECT sensor was tested in the same conditions obtaining a noteworthy response which is superior to values reported in literature. This preliminary in-vitro validation paves the way for a future integration in a portable or wearable architecture.



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Engineering of Light Sensitivity in Chlamydomonas reinhardtii

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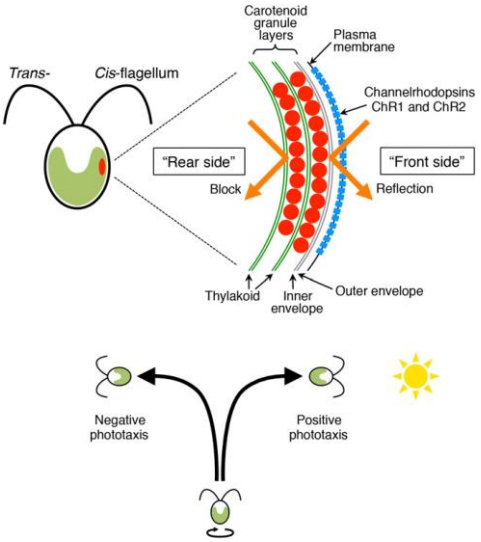
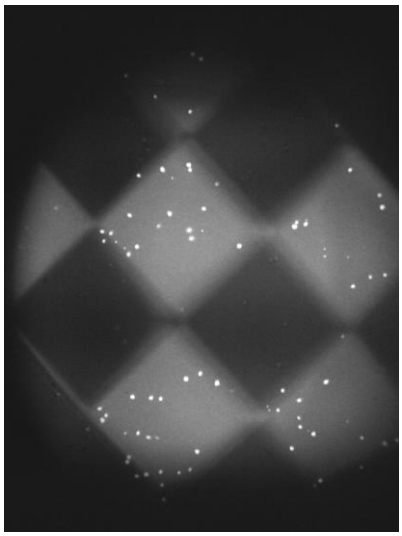
The evolutionistic competence of certain organisms, such as bacteria and algae, to transform energy into motion can be exploited to perform tasks even in highly viscous and hard-to-reach locations, i.e. human organs and tumours. This implies that control over their motility at high spatiotemporal control represents a formidable challenge, which would enable the development of truly bio-compatible and bio-inspired swimmers that can be used for therapeutics and diagnosis. Furthermore, the study and modulation of motion in these organisms allow the unveiling of essential information about cell motility, cell-cell communication, and response to external stimuli. In our studies, we engineer light sensitivity in algae through exogenous phototransducing materials that can interface with the target organism based on non-covalent interactions only, and without the need for genetic transformation. Our model organism is the unicellular microalgae Chlamydomonas reinhardtii, which shows natural fluorescence from chlorophyll and both positive and negative phototaxis[1,2]. The phototransducing materials are polythiophene nanoparticles and azobenzene photoswitches[3], which can transform light energy into electrical potential, thus acting as an artificial eye apparatus. We employ fluorescence microscopy to quantify cell trajectories, migration patterns, and interaction dynamics within the cellular environment with high spatiotemporal resolution[4,5]. Our research aims at engineering light sensitivity in microorganisms, to uncover the interplay between external cues and cellular dynamics, with implications spanning biotechnology, medicine, and beyond.





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Innovative EFOT-Based Time Temperature Integratore for Food Cold-Chain Monitoring

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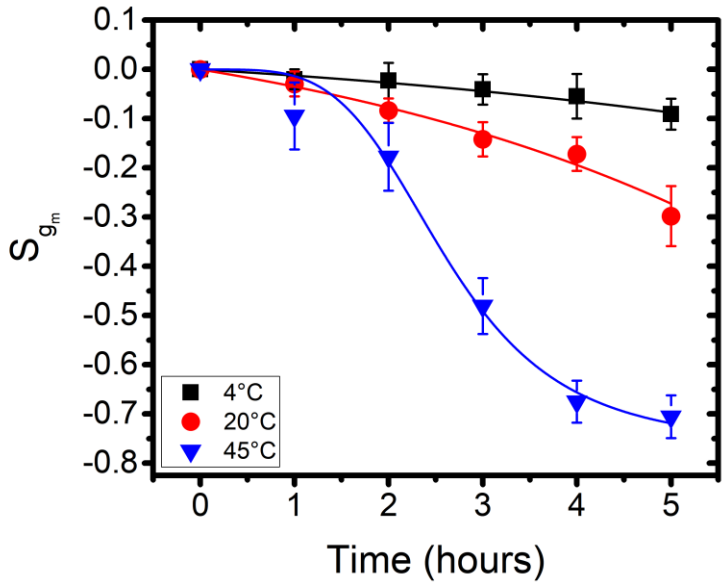
Cold chain relies on keeping perishable goods such as fresh food at a constant, controlled, and low temperature from the point of production to the point of consumption. Any break in the cold chain, such as temperature deviations, can compromise the safety and freshness of the products, leading to food spoilage and even health risks. As technology advances, smart packaging(1) and temperature-monitoring devices such as time-temperature integrators(2) (TTIs) are becoming increasingly important in the cold chain to enhance control, reduce waste, and ensure the overall efficiency of the system. In the view of the FRUALGAE European Project, we developed an innovative TTI based on an electrolyte gated transistor (EGT) and a conductive hydrogel based on reduced graphene oxide(3). The fabricated hydrogel shows a time-temperature dependant irreversible response caused by different dehydration rates. As the hydrogel is exposed to different environmental conditions, each time the hydrogel is then used as gate electrode since its modulation capability changes depending on exposure time and condition. Transconductance signal enables us to discern the time and temperature of exposure of the hydrogel. After further optimization and integration in food packaging, the device could be in principle used to determine the temperature history of fresh food.



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Light-assisted polymerization of electroconductive hydrogels for bioelectronic interfacing

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In the expanding field of organic bioelectronics, conductive hydrogels are emerging as key materials for the development of tissue-like and seamlessly integrated electronic devices. Hydrogels, which are hydrophilic cross-linked polymeric networks, serve as an effective bridge between traditional rigid electronics and soft-nature biological tissues and organs, thus addressing the inherent mechanical mismatch. These polymers are typically insulators but can be engineered to obtain electroconductive blends. Polymeric electroconductive materials, such as poly(3,4-ethylenedioxythiophene) polystyrene sulfonate (PEDOT:PSS), are introduced as electroactive component to craft pristine or doped polymeric conductive hydrogels overcoming conductive inorganic materials limitations. Despite the enormous progress in the organic bioelectronics field, engineering of 3D patterning of conductive polymer materials at micro and nanoscale and the combination of biological and physical stimuli to better mimic the biological environment remains a challenge. Typically, conductive polymers are non-photo-patternable, requiring soft lithography to create 3D structures, which limits architectural and geometric precision. Light-assisted fabrication can overcome these limitations, enabling rapid prototyping of scaffolds and microelectrodes. To this aim, an electroconductive and photo-patternable hydrogel based on gelatin and PEDOT:PSS is presented in this work. Gelatin, modified with methacrylate groups, serves as photo curable material with bioactive features and tunable mechanical properties, while PEDOT:PSS acts as the electroconductive element. The obtained blend has been 3D photo-patterned exploiting two photon polymerization lithography. The resulting 3D structures has been characterized by optical and electron microscopy and electrochemical measurements. Mechanical properties and topological features were investigated by means of atomic force microscopy. The obtained blends can be exploited to develop electroconductive photocured hydrogels at macro-, meso- and micro-scale. It is possible to modulate the system's impedance by changing the amount of PEDOT:PSS in the blend. Finally, biocompatibility assays were carried out with neuronal cells. HT-22 cells cultured on patterned hydrogels showed high viability. Additionally, ongoing investigations are exploring the use of these hydrogels with primary neurons to develop devices that can be integrated into the brain or utilized as platforms for in vitro neuronal studies. The proposed approach offers a promising pathway for creating fully organic and bioactive 3D electrodes with controlled morphology for sensing and stimulating cells and tissues. The material developed can be employed to craft devices at different length scales addressing specific needs depending on the application, from tissue engineering, electrode coating and 3D scaffolding for cells and guided neurites outgrowth.

Development of a salivary uric acid sensor for health status monitoring

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Uric acid (UA) is a relevant biomarker associated with health status. In particular, it is the major antioxidant component in saliva, consequently UA concentration can be exploited to estimate oxidative stress.[1] This condition is defined as an unbalance between the production of reactive oxygen species (free radicals) and antioxidant defences and has been linked to a wide range of health problems including cancer, cardiovascular and neurodegenerative diseases. In this contribution, we present the development of a chemical sensor based on organic electrochemical transistor (OECT) for uric acid selective monitoring in saliva. The transduction mechanism exploits potentiodynamic technique to evaluate the transconductance peak (gm) as the analytical signal and guarantee a high selectivity (Fig.1). Sensors are fabricated with poly(3,4-ethylenedioxythiophene):polystyrene sulfonate (PEDOT:PSS) thus benefitting of the polymer capability to catalyze analytes electro-oxidation. UA is detected with the OECT sensor, by means of its oxidation occurring at a gate voltage within PEDOT:PSS stability window.[2] Device structure and performances were optimized resulting in a sensitivity of (62 ± 5) µS dec-1, high repeatability and reproducibility, respectively 5% and 8% expressed as relative standard deviation, and a limit of detection of 1 µM. The measurements were then carried out in human and swine saliva, showing the possibility of exploiting the device for analysing real, complex and destructive samples. The results were compared to a commercial enzymatic assay kit for salivary uric acid: UA concentration in human saliva estimated with OECTs was statistically equivalent to the one assessed with the commercial kit ($(3.4 \pm 0.2) \times 10^2$ µM) demonstrating the accuracy of the detection and validating the method. The small, lightweight devices can be easily integrated into portable electronics to further simplify the setup and reduce costs.

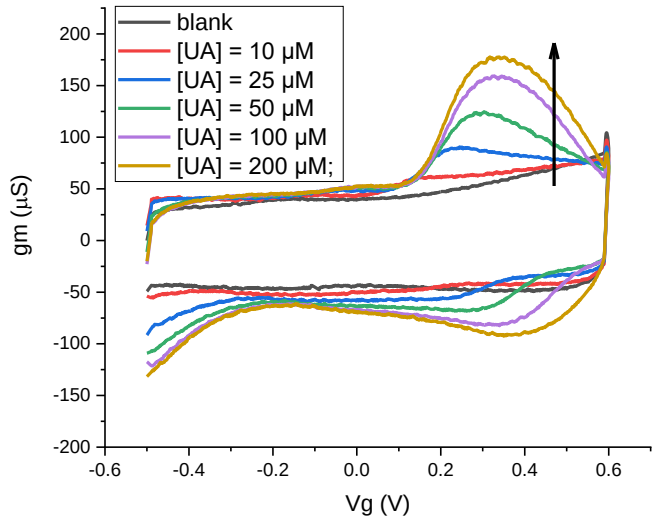

Figure 1. Transconductance curves in PBS 0.1 m (pH 7) at increasing uric acid concentration.

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Organization of *β*-Adamantylmethyl-modified Polythiophenes determined by Self-Assembled Monolayers – A study of epitaxial effects

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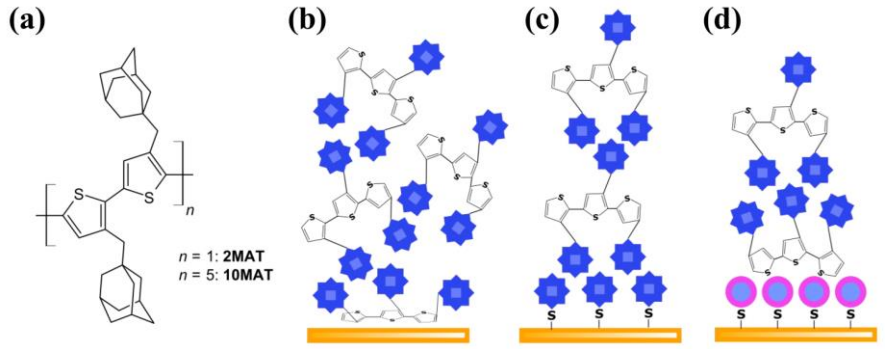
The anisotropic charge transport in organic materials necessitates precise control over their self-assembly, especially in conductive polymers like poly(3,4-ethylenedioxythiophene) PEDOT.[1] Achieving outstanding conductivity in PEDOT-based devices has involved various methods such as solution shearing, acid treatment, strong doping agents, self-doping, etc. These efforts have led to a conductivity record of 8 797 S cm^{-1}.[2] Recent approaches have succeeded even without added oxidants. The success of the PEDOT material is due to its ability to form stable, planar intra-molecular bonds, which suppress disorder and enhance 2D transport. Notably, high-performance organic semiconductors have been trending towards thinner forms, with nanowires formed on highly controlled surfaces achieving record conductivities.[2] This has highlighted the significance of the epitaxial effects of substrates. Studies showed that using self-assembled monolayers (SAMs) with different head groups on gold surfaces could drastically change topographies and surface potentials.[3]

This work uses recently published poly(3-adamantylmethylthiophene) (PMAT)[4] in two isolated fractions (dimer **2MAT** and decamer **10MAT**) to explore these effects, comparing its self-assembly on two different SAMs with distinct head groups during spin-coating. PMAT showed different self-assembly modes on bare gold Au(111), mica, and glass, suggesting varied interactions. The findings confirm the utility and potential of epitaxial effects and adamantyl substituents to enhance organic electronics, primarily through improved performance of the resulting electronic devices.



MAT fractions obtained	2MAT	10MAT
Mn [g mol-1]	400	552
Mw [g mol-1]	581	2 613
Dispersity [-]	1.45	4.73
Approx. number of units [-]	**2**	**10**

(a) *Chemical structure of PMAT and the respective chain-length for 2MAT and 10MAT.* ***(b-d)*** *Illustration of envisioned epitaxial effects on self-assembly of PMAT-trimers on gold surfaces:* ***(b)*** *bare gold,* ***(c)*** *AD-SAM, and* ***(d)*** *PH.* ***(e)*** *Properties of PMAT-based oligomers measured via GPC.*

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Determination of stiffness and elastic modulus of 3D printed micropillars with AFM Force Spectroscopy

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Currently, numerous applications across various fields such as optics, tribology, biology, and biomedical engineering are leveraging micropillars.[1] Among these, one of the most appealing uses is in three-dimensional microelectrode arrays for in vivo and in vitro studies, including cellular recording, biosensors, and drug delivery.[2] Depending on the application, the optimal mechanical response of micropillars can range from soft to stiff. For long-term implantable devices, it is crucial to avoid mechanical mismatch between the micropillars and biological tissue. For drug delivery patches, micropillars must penetrate the skin without breaking or bending. Accurate mechanical characterization of micropillars is essential in the fabrication and optimization of these devices, as it determines their success or failure.[3-4] In this poster session, we report an experimental method based solely on AFM force spectroscopy that measures the stiffness of a micropillar and the elastic modulus of its constituent material. We tested our method on four different types of 3D inkjet-printed micropillars: two silver micropillar sets sintered at 100 and 150°C, respectively, and two polyacrylate micropillar sets with and without a metallic coating. The estimated elastic moduli were found to be comparable to their corresponding bulk values. Moreover, our findings indicate that neither the sintering temperature nor the presence of a thin metal coating significantly influence the mechanical properties of the micropillars.

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Neuro-inspired conductive polymers: material strategies for neuroelectronics

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The field of neuroelectronics aims at engineering electronic platforms that can interact with neurons and the brain in order to stimulate and record electrical activity for a deeper understanding of neuronal communication and functions. Given the extremely complex nature of neuronal networks and environment,[2] it is crucial to realize electronic devices inspired by the neurons and the brain itself for a seamless integration. In this scenario, recently conductive polymers, e.g. PEDOT:PSS, have gained increasing attention thanks to their advantages, as compared to conventional electronics, such as biocompatibility and facile chemical functionalization.[1] However, existing polymer-based devices are not yet able to effectively mimic and reproduce the complex neuronal environment, being flat and bidimensional, as well as reproducing specific electrical functions.

Here we introduce material strategies to achieve bio-inspired PEDOT-based neuroelectronic platforms that mimic the neuronal shape, mechanical properties, and electrical function. The neuronal shape was reproduced by the formation of PEDOT:PF_6 dendritic-like fibers employing AC electro polymerization[3] on multi electrode arrays (MEAs). By changing the parameters of the applied signal, the growth and morphology of the fibers were altered. The soft mechanical properties were mimicked by realizing electroconductive hydrogels composed of PEDOT:PSS blended with a modified photo-patternable gelatin.[4] The so obtained conductive hydrogels were 3D photopatterned via two-photon-polymerization (2PP) lithography[5] for the fabrication of microstructures as cell-instructive scaffolds and topographical cues. Lastly, electrical function such as short- and long-term plasticity was emulated by introducing an ion-binding moiety on the PEDOT backbone, namely crown ether,[6] that represents ion channels, crucial components of the plasma membrane of biological synapses involved in the electrical neuronal communication. The PEDOT-Crown was electropolymerized in the presence of ClO_4^- as counterion and dopant and integrated onto an organic electrochemical transistor (OECT) as neuromorphic platform.

All the investigated materials were morphologically characterized by means of scanning electron microscopy (SEM) and optical microscopy. Additionally, the electrochemical properties of the obtained materials were investigated via electrochemical impedance spectroscopy (EIS) and cyclic voltammetry (CV). Finally, biocompatibility assays were carried out for both dendrites-like fibers and PEDOT:PSS hydrogel.

In conclusion, the proposed strategies allow for the fabrication of neuroelectronic devices and electrodes with different levels of complexity that can effectively mimic neuronal features. Such systems will open the way to the possibility of sensing and/or stimulating cells and tissues in a more realistic environment.

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Fully Passive Electrochemical Oxygen Sensor Enabled with Organic Electrochemical Transistor

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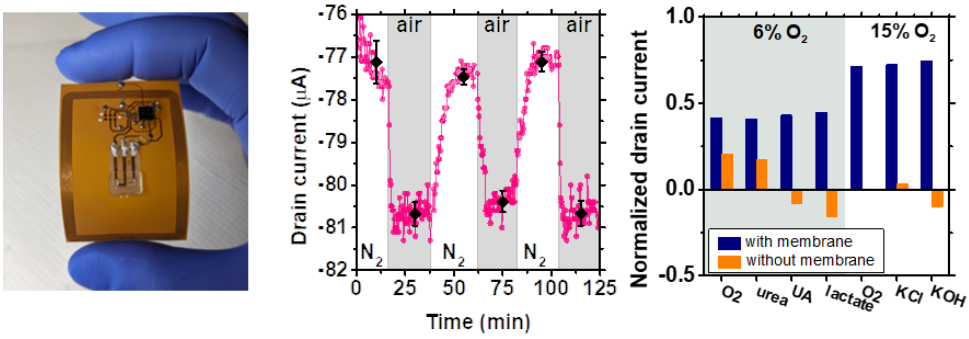
This work presents the development of a fully passive electrochemical oxygen sensor enabled by Poly(3,4-ethylenedioxythiophene):poly(styrenesulfonate)-based Organic Electrochemical Transistors (PEDOT:PSS-based OECTs). This sensor combines the high sensitivity, low-voltage operation, and stability of OECTs with the biocompatibility and low-cost fabrication of PEDOT:PSS on flexible substrates like textiles and plastics.[1,2] Moreover, it offers a solution for continuous, battery-free oxygen monitoring for applications in medical diagnostics, environmental monitoring, and industrial safety.[3]
We investigated the optimization of OECT-based sensor geometry and structure to ensure reliable integration with commercial battery-free Near Field Communication (NFC) readouts. This effort addresses the challenges posed by high channel currents and extended operation times (>1 min) required for obtaining reliable, quantitative results, which typically lead to increased energy consumption. Here, we propose a hydrogel-based PEDOT:PSS OECTs[4,5] encapsulated in a silicone-based membrane serving as battery-less oxygen sensors for both liquid and gas environments. Our results highlight the importance of device miniaturization and hydrogel electrical properties in achieving reliable passive operation. Furthermore, we demonstrate an enhanced stability of the sensing process provided by a selective oxygen-permeable membrane that allows for reliable oxygen detection even in complex biological mixtures, including oxidizing analytes.

Passive and interference-free OECT operation for oxygen sensing



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PEDOT:PSS OECTs as versatile devices for real-time monitoring of cytotoxicity and viral infection

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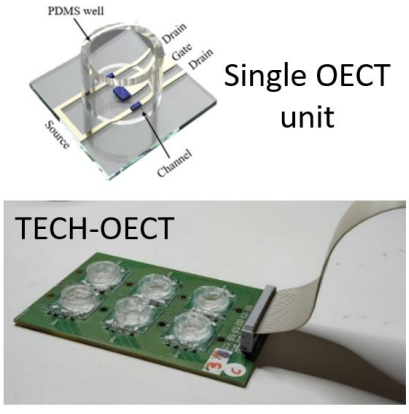
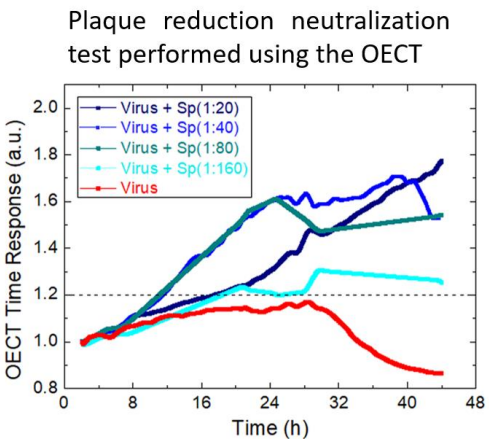
Semiconducting polymers are promising materials for biomedical application due to their ability to conduct both ions and electrons, their biocompatibility and their flexible and soft mechanical nature. In particular, poly(3,4-ethylenedioxythiophene):poly(styrenesulfonate) (PEDOT:PSS) has high conductivity and reversible electrochemical properties in acqueous environment making it suitable as smart biointerfaces with biological entities.

Here, we present PEDOT:PSS-based Organic Electrochemical Transistors (OECTs) for the electrical continuous monitoring of cell viability, providing fast and real-time outputs which overcome standard optical-based techniques, without the need of toxic substance staining or highly-specialized operators. Cells are directly grown on transparent, PEDOT:PSS-based thin film OECTs: the presence of a cell monolayer slows down ion flux from the electrolyte into the semiconducting polymer, allowing for an electronic readout of cell layer health. We demonstrated that the devices can evaluate in real-time cytotoxicity of external agents, viral infection pathway on cell and titration.[1] Moreover, testing Sars-Cov-2 infected cells, we observed that OECTs can automatically quantifying neutralizing antibodies in human sera in less than 48h.[2]

PEDOT:PSS OECTs provide a scalable, low-cost and versatile biosensor for monitoring cell culture stress response, paving the way for high throughput drug discovery screening, toxicology evaluations, and serum neutralization assays.





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Electrogelation: An alternative route for the deposition of PEDOT:PSS and its copolymers for Bioelectronics

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In this study, we utilised electrogelation of poly(3,4-ethylenedioxythiophene) polystyrene sulfonate (PEDOT:PSS) and its copolymer with polystyrene sulfonate-co-styrene methenamine (PEDOT:PSS-co-PSMA) to develop conducting coatings for bioelectronic applications. The coatings were used to lower the impedance of silver electrodes, leading to a decrease in the voltage needed to achieve cutaneous stimulation of small fibres and an increase of the signal-to-noise ratio in cutaneous biopotential recordings. Additionally, PEDOT:PSS-co-PSMA was integrated as the gate electrode in an organic electrochemical transistor (OECT), showing improved performance compared to non-modified and electrogelated PEDOT:PSS and plain gold electrodes. The results show that electrogelation offers a scalable and cost-effective solution for depositing conducting polymers, even enabling the deposition of non-solution processable polymers, as performance-enhancing coatings for bioelectronic applications.

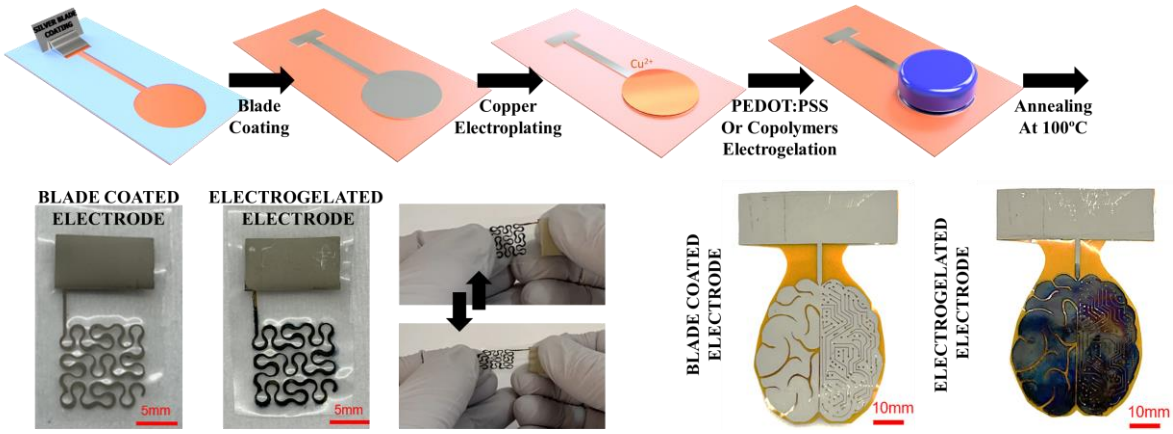

Figure 1. (TOP) Scheme of the manufacturing process: first silver nanoparticle paste is blade coated on the substrate *e.g.* Kapton, using blue tape as a mask. Then, copper as a sacrificial layer is electroplated on the silver electrode. Subsequently, the electrode is immersed in 10 v/v% PEDOT:PSS dilution and the copper oxidized at 0.5 V forming a gel, finally the gel is collapsed via annealing for 5 min at 100ºC. (BOTTOM) Examples of electrodes bladed coated with silver ink (grey) and its post electrogelated (blue) on flexible polyurethane (left) and Kapton (right)

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Organic electrochemical transistors based on electro-polymerized channel for selective Zn ion detection

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Organic electronics have been widely used for biological applications.[1] More specifically, organic electrochemical transistors (OECTs) are attracting extensive attention recently due to their large transconductance that offers high signal to noise ratio (SNR), thus enabling the detection of weak biological signals.[2] In particular, monitoring ion fluxes through the plasma membrane is highly attractive as it provides important information about the mechanism of different organs such as the pancreas. For example, diabetes is caused by issues with glucose metabolism and insulin regulation by pancreatic islet. Since zinc ions are released with the secretion of insulin by β-cells of pancreatic islet in response to glucose stimulation, finding a way to monitoring these ions is crucial for early detection of diabetes.[3]
To this regard, OECT based Zn^{2+} biosensors have been developed where an organic mixed ionic electronic conductor (OMIEC) selective to zinc cations, 2 (bis(pyridin-2-ylmethyl)amino)ethyl 2-(2,5-bis(3,4-ethylenedioxy thiophene)thiophen-3-yl) named p-Tri-DPA was electropolymerized in the channel. The measured electrical characteristics of the OECT show typical p-type OECT behavior, with transconductance values in order of a few mS, comparable to the state of art of OECTs presented in the literature.[4] Subsequently, transient measurements were recorded and demonstrated the sensitivity of these OECTs to zinc cations (~$1.16x10^{-3}$ µA/µM) (see Figure 1a), and their selectivity comparing to other cations such as Ca^{2+}, Mg^{2+}, K^+ (see Figure 1b) To our knowledge this is the first Zn^{2+} sensor based on OECTs obtained with high sensitivity and selectivity.[5] These devices are now under investigation for vitro biological applications.

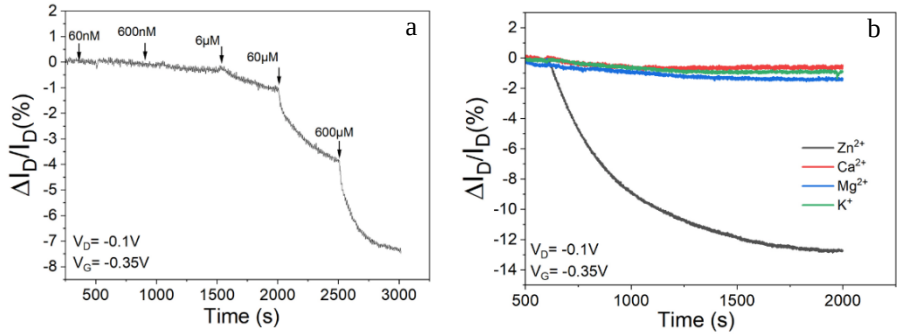

Figure: Selectivity measurements comparing the normalized current response, ΔI_D, for Zn^{2+}, Mg^{2+}, $Ca^{2+}$and K^+ for 550µmol.L^{-1}additions

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The exploring of thin-film transistors (TFTs) technology for novel display, active-matrix sensing and life science applications

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Thin-film transistors (TFTs) have emerged as pivotal components in various technological applications due to their versatility, scalability, and compatibility with large-area manufacturing processes. These advancements in TFT technology underscore the expanding horizons of its application across three distinct application areas through our years of efforts: novel active-matrix display, optoelectronic sensing, and high-throughput on-chip oligonucleotide synthesis. Normal fabrication techniques, such as inkjet printing and chemical vapor deposition on the TFT arrays, enable the scalable production of promising active-matrix perovskite/QLED/OLED displays[1-2]. These displays achieve remarkable color accuracy, high brightness, and low power consumption, thus hold significant potential for applications ranging from consumer electronics to augmented reality systems. In optoelectronic sensing, TFT-based sensors offer unprecedented opportunities for high-resolution, large-area sensing platforms, facilitating applications in x-ray detection[3], biomedical diagnostics, environmental monitoring, security checking and anti-counterfeiting. Moreover, by integrating TFT-enabled electrochemical microarray with a microfluidic system, researchers in LinkZill have achieved precise control over solid-phase DNA synthesis reaction conditions, leading to automatic, high-throughput synthesis of oligonucleotide pools[4]. This on-chip synthesis platform streamlines the process of oligonucleotide design and enables the synthesis of customized DNA sequences thus revolutionizing the applications including gene editing, antibody screening, protein expression diagnostics and drug discovery et, al.

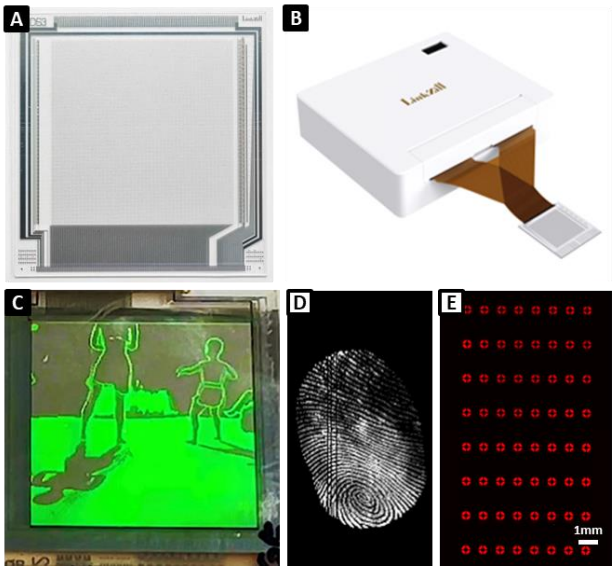

*Figure. (a) Typical active TFT array with resolution 256*256 and (b) driving electronic system, and the demo-show of the (c) QLED display, (d) finger-print recognition. (e) Oligo synthesis results indicating by fluorescent probe hybridization on the base of TFT with resolution 8*8 in LinkZill.*

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Tattoo electrodes are intrinsically breathable

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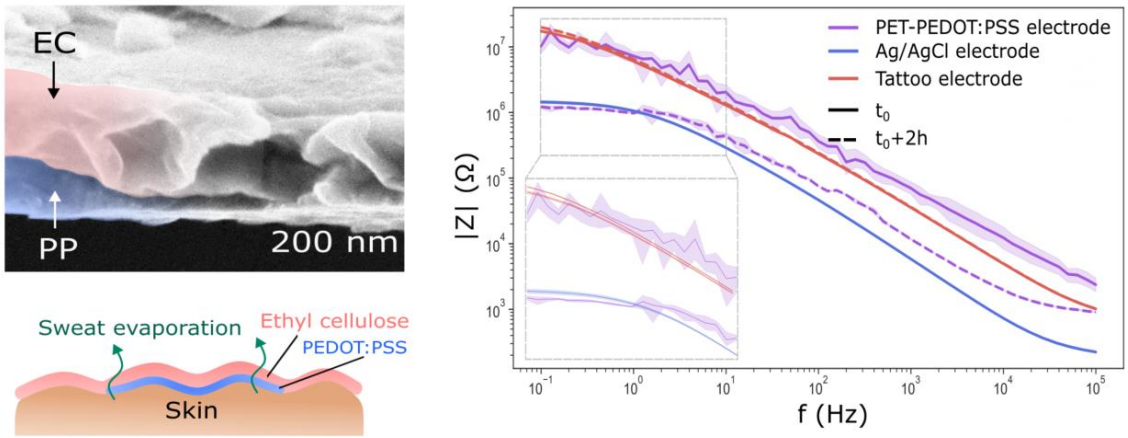
Flexible, soft, and thin organic skin-contact electrodes can acquire surface biosignals with a seamless interface while guaranteeing high quality data However for long-term recordings sensors should also be breathable to ensure physiological trans epidermal water loss (TEWL) and reduce the inflammation risk and discomfort on the user.[1] Generally, plastic and elastomeric electrodes are made porous to enhance their water vapor transmission rate (WVTR).[2,3] To ease and scale up the manufacturing process, intrinsically breathable films would represent the ideal material. In this context, tattoo sensors not only exceptionally conform and self-adhere to the skin thanks to their ultralow thickness (~ 1um), flexibility, and softness, but are also made by materials with high permeability. Here we quantitatively report on the breathability of tattoo sensors made of ethyl cellulose and PEDOT:PSS. SEM and AFM micrographs revealed the presence of internal cavities. The liquid water permeance assessments confirmed tattoos function as compressible porous membranes. The water vapor permeability measurement resulted in a transmission rate remarkably higher than the physiological TEWL. Ultimately, the comparison of electrochemical impedance spectroscopy spectra of tattoo-, gelled-, and plastic- electrodes demonstrated a stable dry interface between tattoos and skin over time. With this study we extensively elucidated the properties of polymeric tattoos sensors that make them suitable as breathable epidermal devices optimal for prolonged and high-quality biosignals recordings [4].



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Spray-coated poly-3-hexylthiphene on planar and three-dimensional surfaces: first studies about the cellular behavior

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For a long time the *in vitro* models were based on planar surface and the topography of the cells' environment was considered an irrelevant aspect. However, recent developments have shown that how cells react to the environment influences their morphology and activity. Thus, for the advancement of *in vitro* model systems, the field of bioelectronics is moving a step forward in the study of material that can better interact with living systems.[1] In this instance, particular attention is given to the design of organic bio-interfaces with microstructures such as nanoholes, groves and micropillars that recall the cell's environment with its fibrils, holes and pits. These microstructures can influence the cleft width between the cell membrane and the substrate, and affect the cell's adhesion and morphology.[2] Among the most studied organic semiconductive materials, poly-3-hexylthiophene (P3HT) is notable, having been previously used for organic solar cells[3] and then for *in vitro* and *in vivo* applications.[4,5] The potential of this polymer lies not only in its biocompatibility but also to its ability to absorb visible light (300-700 nm with a pick at 520 nm) through which it can be used for the modulation of the cell activity.

This work aims to study not only how the cells interact with a pseudo-3D structure, but also how they behave in the presence of the same structures covered by a film of P3HT.To do that the P3HT is sprayed on silicon-based planar (2D) or micropatterned materials (3D). The obtained samples are characterized by the cyclic voltammetry and the impedance to determine their ability to react and develop the current after an optical stimulation. A live-dead assay is performed to assess the biocompatibility of the P3HT polymer and then with scanning electron microscopy (SEM) the adherence and the morphology of the cells are studied. The previous results show that the samples covered by the P3HT film have good conductivity and are biocompatible. Moreover, morphological studies show how well the cells interact with the two different topographies of the surfaces covered and not covered with P3HT with a particular preference for the pseud-3D structure. This opens the way to the potential application of this 3D P3HT interface for the optoelectrical stimulation of cells modulating not only their interaction with the surface of interest but also their electrophysiological activity.

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Neuromorphic Organic Electrochemical Transistors: PEDOT:PSS Electrochemical Polymerization on the Gate Electrode for High-Endurance Long-Term Potentiation

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Organic electrochemical transistors (OECTs) are gaining momentum as devices for artificial intelligence, as they are able to emulate short-term synapses functionalities (short-term plasticity, spike-dependent plasticity, etc..) thanks to the peculiar features of OECTs ionic circuit. On the other hands, long-term potentiation (LTP) must be further developed to increase the retention of the induced neuromorphic states[1].

This contribution describes an innovative approach (Figure 1) to exploit electrochemistry to emulate long-term potentiation of neuron with an OECT[2]. The gate voltage acts as presynaptic signal (V_{pre}) and induces the electrochemical deposition of PEDOT:PSS film. The consequent increase of gate capacitance raises the ability of the gate electrode in modulating the current flowing in the channel, which is the post synaptic signal. LTP depends on both the number of pulses used and the V_{pre}, which generates LTP when a threshold of +0.7 V is overcome. The synapse weight is evaluated by measuring the transconductance, which varies from 0.3 µS for the native device to 30 µS for the neuromorphic OECT with the highest LTP. In-operando atomic force microscopy shed light on operating principle by showing the modifications of the gate electrode. The structural strengthening of the artificial synapse is stable for at least two months, and the behavior can be reset by inducing long term depression by applying gate voltages pulse that leads to a PEDOT:PSS overoxidation and to the formation of a nonconductive layer on the gate electrode. The artificial synapse also mimics short-term plasticity, and in particular paired pulse depression.

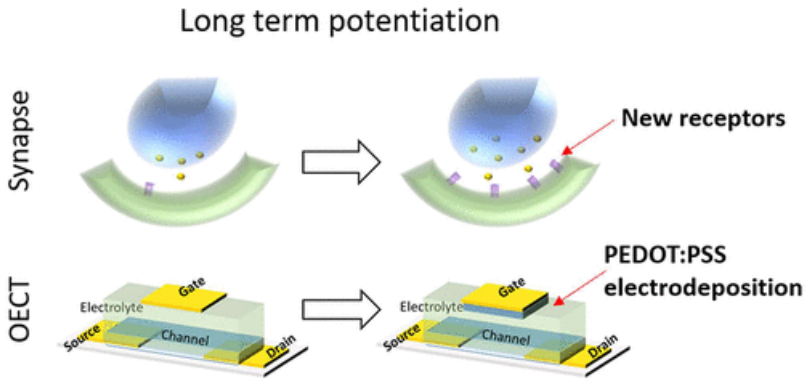

Figure 1: Sketch that describes the operating principle of neuromorphic OECT by highlighting the analogy with neurons

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Liquid-gated Transistor Based on Graphene Acetic Acid for Histamine Aptasensors

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Liquid-gated transistors (LGTs) are electronic devices operating in a liquid medium such as Milli-Q water or saline aqueous solutions. These devices comprise three terminals sharing the liquid medium. Two of them, the "positive" (**P**, source of holes) and the "negative" (**N**, source of electrons), are channelled by a material—either a semiconductor or a semimetal. Either **P** or **N** are grounded: presuming the former as the ground, two biases can be independently applied—a **N**-*vs*-**P** bias ($\mathbf{V_{NP}}$) and a **G**-*vs*-**P** bias ($\mathbf{V_{GP}}$).[1]

Both $\mathbf{V_{GP}}$ and $\mathbf{V_{NP}}$ influence the verse and intensity of the electrical current crossing the channel material ($\mathbf{I_{Channel}}$). $\mathbf{V_{GP}}$ yields two electrical double layers (EDLs) formed in the liquid medium: the first involves **G** and the solvated cations (or anions, if $\mathbf{V_{GP}}$ is positive); the second occurs between the channel and the solvated anions (or cations, if solvated anions gather close to **G**). In turn, changes in the second interface also alter the conductivity of the channel material and, as such, $\mathbf{I_{Channel}}$.[1]

The channel-solution interface can also be tuned by embedding molecules inside the channel material. To endow the LGTs with sensing capabilities, biomolecular receptors are commonly embedded.[2] In such a way, charge-distribution alterations alongside the channel-solution interface take place when the receptors recognise their target dissolved in the liquid medium. Thereby, LGTs can give out intelligible electrical readouts out of the receptor-target recognition.[1]

In this work, we first propose a strategy to design LGTs integrating graphene acetic-acid (GAA) as the channel material. We deployed dielectrophoresis (DEP) as the deposition means of the GAA. DEP relies upon alternating-current (AC) stimuli imparted towards **P** and **N**. Meanwhile, an aqueous suspension containing particles of GAA wets the **P** and **N**. The AC yields a gradient of the electrical field that polarises the particles and relocates them towards the **P**-**N** interspace.

GAA includes acetic-acid branches bound to the sp^2 carbon frame. Aside from conferring water processability to the GAA,[2] the acetic-acid branches afford the chemical functionalization of GAA. For instance, the 1-ethyl-3-(3-dimethylaminopropyl)carbodiimide/N-hydroxysuccinimide (EDC/NHS) click chemistry can be harnessed to activate the acetic-acid moieties and, afterwards, exploit them to anchor amino-substituted compounds onto the GAA.[3] In this regard, we took advantage of the EDC/NHS approach to graft ethanolamine onto the GAA as a benchmark. The successful outcome of this approach was corroborated by comparing the X-ray-photoelectron-spectroscopy (XPS) C1s signals of GAA beforehand and after its functionalisation.

Presently our efforts are focused on creating a GAA-based LGT aptasensor towards histamine. With the same concept outlined before, we took advantage of EDC/NHS chemistry to connect the GAA with amino-terminated aptamers—the receptors of interest. We employed electrochemical impedance spectroscopy (EIS) as a first characterisation tool to establish the surface functionalisation of GAA with the aptamers. Preliminary sensing tests were carried out by using benchmark solutions of histamine. These tests were performed on pristine GAA LGTs—aiming to find out whether histamine interacts aspecifically with the DEP-deposited GAA.

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Design and characterization of soft tissue-mimicking hydrogels for bioelectronics coatings and substrates

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Soft biomimetic materials are increasingly used in biomedical applications for tissue engineering, drug delivery systems or as agents for wound dressing. Novel composites and fabrication methods enable the possible use of these materials for coatings of bioelectronics or directly as substrates[1]. The requirements for such materials are demanding and diverse and include physical, chemical and biological aspects of material design and characterization[2]. Specifically, the mechanical match between biomimetic material and tissue depends on the macroscopic mechanical properties and morphology of the bulk material as well as on the surface and interface properties. Additionally, chemical stability and degradation control, especially in biological environments, are crucial for the proper functioning of coatings or substrates. In addition to functionality, coating materials or substrates must be compatible with the biological host. To prevent toxic or adverse effects, the release of substances from the material to the host must be controlled and well-understood in all phases. Although often reduced to compatibility with cells, biocompatibility is determined by the combination of all of these physical, chemical and biological factors.

We demonstrate an ultra-soft, porous and organic hydrogel based on polyvinyl alcohol that can be used as a coating and device substrate[3]. Our focus here is on the biomechanical characterization of the bulk properties and on the surface and interface properties. First, we introduce the optimization of the fabrication of sterile materials. The biomimetic properties are assessed through new biomechanical experiments comparing the mechanical stiffness, material porosity and fluid permeability to those of biological soft tissue. The mechanical behavior is related to the microstructure using cryo-electron microscopy and various histological investigations. Based on the information from material characterization, we assess the bioadhesion properties of material variations on biological membranes. Finally, we introduce prototypes of bioelectronic devices (see Fig.1) based on this biomimetic material and emphasize its general biocompatibility and potential usability across various scales and biological species.

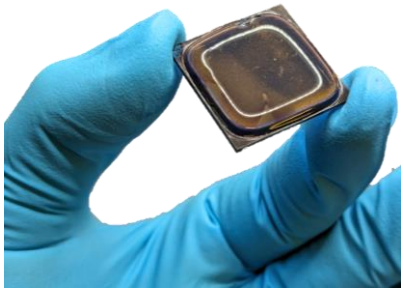

Figure 1 Prototype of an optoelectronic cell with soft tissue biomimetic hydrogel coating.

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Tailor made organic semiconductors with bio-inspired side chains for organic bioelectronics

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Organic semiconductors form the basis of a constellation of electronic devices such as organic light-emitting diodes, organic field-controlled transistors or solar cells. Based on organic transistors, devices were developed, laying the basis of organic bioelectronics. The aim of organic bioelectronics is to develop technologies and materials that can integrate, probe and influence biological systems and form contact between biotic and abiotic environments. Research in organic bioelectronics is leading to the development of a wide range of applications, from biosensors and drug delivery systems to health monitoring devices at the brain-artificial interface. Performance of a conducting polymer can be improved by tailoring of the side chains which may enhance solubility (processability), mixed ion-electron conductivity and biocompatibility. For bioelectronic applications, improvement of the biocompatibility can be achieved by an additional biocompatibilizing layer (e.g. polylysine[1]), which, however, may lead to delamination of the layers, or covalently linking polypeptides such as RGD[2] or amino acids[3]. Proper molecular design and development of selective and efficient synthetic methodologies will be able to overcome the existing disadvantages of such materials, namely often low conductivity, sensitivity, stability, or biocompatibility. This work is dedicated to the synthesis of a series of semiconductive polymers and copolymers with a new bioinspired side chain. The side chains of the synthesized polymers carry the amino acids, which are linked to the main chain by glycol linkers of various lengths. The target polymers exhibit good solubility in polar solvents like ethanol and methanol, stability in water and thermal stability up to 100 °C. The studied compounds establish a platform for new class of materials for organic-electrochemical-transistor devices (OECT) for biosensing and other applications in organic bioelectronics.

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Effect on the Donor Moieties on Emission Properties and OLED Performance of Tetra Substituted Ethylene Derivatives

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Excited state relaxation dynamics of organic multibranched donor-acceptor derivatives control the efficiency of optoelectronic devices[1-3]. In this work, emitters with various donors (tBu-carbazole, acridine and phenoxazine) attached to the tetraphenylethylene (TPE) stator core were designed and synthesized using McMurry and Buchwald-Hartwig methods. The series of the compounds were investigated for their potential as yellow/green emitters and hole transporting materials for OLEDs. Photoluminescence quantum yields in the solution state of the compounds ranging from 8.09% to 83.58% were observed. The presence of various donor moieties in TPE affected the device efficiencies. The presence of multiple donor units resulted in good thermal stability and hole transporting capabilities making them suitable for effective OLED applications.

Acknowledgment:

Kuppusamy Santhiya thanks the Lithuanian Research Council for a postdoctoral fellowship (S-PD-22-105).

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The Crucial Role of Cell/Polymer Interface for the Transduction of Action Potentials via Printed Electrolyte-Gated Polymer Field-Effect Transistors

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Electrolyte Gated Field-Effect Transistors (EGFETs) based on conjugated polymers have emerged as fundamental building blocks in bioelectronics due to their ability to convert weak biological signals into amplified electronic outputs while operating stably in aqueous environment.

Conjugated polymers exhibit biocompatibility and 'soft' mechanical property thus favouring direct coupling with biological cells, tissues and organs. As such, EGFETs have been used for monitoring cell cultures and for electrophysiological recording of excitable cells such as neurons and cardiac cells. In such applications, cells are directly plated onto the active channel of the transistor that is comprising of an organic polymer coated with a porous protein to enhance cell adhesion. Therefore, ion fluxes due to the electrical activity of the cell such as the Action Potential (AP) is directly coupled to the EGFET resulting in a modulation of the channel conductivity that is measured in transistor current modulation. While it is true that the amplification factor of EGFET has to be maximized to provide large local amplification of the bio- signals, recording the accurate signal of the action potential however goes beyond the device intrinsic electrical parameters.

In this context, I will present our latest results where we employed an EGFET made of different conjugated polymers to record the action potential of a 2D layer of human induced Pluripotent Stem Cell-derived Cardiomyocytes (hiPSC-CMs).

Interestingly, we observed that depending on the active polymer employed as active channel for the EGFET, the recorded AP has the shape of either an intracellular–like or a Field Potential (FP) as recorded using simple microelectrodes. Surprisingly, an EGFET with a much lower transconductance could transduce the AP signals much more accurately than an EGFET with a large transconductance. This indicates that the electrical coupling between the cell and the transistor channel predominantly relies on the interface between the cell membrane and the polymer at the cleft.

N-doped carbon dots as sustainable materials for optical modulation of plant and animal cells

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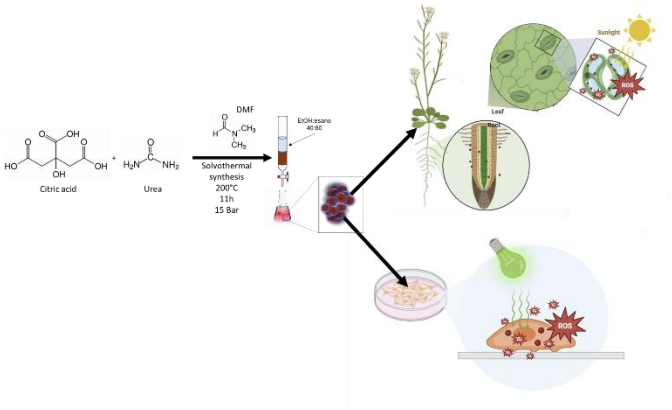
In recent years, the development of carbon dots (CDs) has gained significant attention due to their exceptional properties and potential applications in various fields[1]. As a sustainable and environmentally friendly material, carbon dots offer a promising alternative for bioimaging, drug delivery, and agricultural applications[2]. The present work exploits the optical properties of N-doped carbon dots to photoinduce coupling mechanisms between CDs and a biological environment, both in animal cells and in plants.

Here, we take advantage of the eco-friendly, one-step hydrothermal synthesis method, to realize sustainable CDs. We provide extensive characterization of their optical and electronic properties, showing their photocathodic behaviour in an aqueous electrolyte. After assessing the lack of cytotoxicity, we demonstrate the effectiveness of CDs in modulating the cellular response through the production of reactive oxygen species (ROS) in both animal and plant cells. Finely tuned, on demand modulation of ROS pathways may represent a breakthrough in precise control of biophysical pathways in both plant and animal cell models. Overall, the great potential of CDs suggests that they will be suitable materials for advancing sustainable technologies in biomedicine and precision agriculture.



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Inkjet printed metallic micropatterns for electroanalytical applications

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The ocean represents a huge ecosystem on Earth, and almost all its biomass is composed of microorganisms. These microorganisms, more commonly known as plankton, are of crucial importance both for marine organisms, as they form the basis of the marine food chain, and for terrestrial organisms, as they are responsible for 50% of the Earth's annual oxygen production[1]. Unfortunately, there is currently no efficient method to analyse them and study their population variation.

The objective here is to separate these microorganisms on the basis of their morphological characteristics. This research concerns the development of a device dedicated to the separation of colloidal suspensions flowing at high speed by dielectrophoresis[2,3]. Two substrates, on which the electrodes are printed by inkjet, are positioned opposite each other to form a channel, in which the solution flows. By optimising the intensity and frequency of the sinusoidal voltage applied, it is possible to control the trajectory of the particles according to their size for polystyrene particles (500 nm-1 µm) or their nature for algae (separation of *Alexandrium minutum* and *Prorocentrum micans*)[4]. In addition, the use of printing processes, makes it possible to increase the surface area of the substrates (without modifying the height of the channel), allowing the formation of a network of 16 channels in parallel and thus to obtain a separation of particles at a previously unattainable flow rate (150 $\mu L.min^{-1}$) and to trap particles with a diameter of 500 nm[4].

The dielectrophoretic force is directly related to the inter-electrode distance: the smaller the distance, the stronger the force. To achieve better handling of small particles (500 nm and smaller), it is necessary to reduce the inter-electrode distance in order to increase the electric field gradient. For this reason, an approach has been developed to overcome the resolution limits (distance between two electrodes) of inkjet printing. The method is based on controlling the drying dynamics of functionalised SiO_2 nanoparticle suspensions[5]. Microstructures are obtained and form a template for silver ink printing. This strategy makes it possible to increase the printing resolution by an order of magnitude and thus to obtain gaps between two silver lines of a few micrometres by inkjet printing.

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Dendritic Growth of 2.5D PEDOT Fiber Electrodes for Neuroelectronic Applications

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In the field of organic neuroelectronics, the use of conductive polymers shows promising results for the application in biological interfaces, because of their biocompatibility and mixed ionic and electrical conduction. These devices were shown to have neuromorphic properties emulating the synaptic plasticity of biological neuronal networks.[1] Furthermore, they exhibit the ability to be integrated with cells and show response to neurotransmitters.[2] However, they do not exhibit the 2.5D/3D features, characteristic of neuronal cells. Recently, a new fabrication process exploiting electro polymerization has shown great potential in resembling dendritic structures through the growth of PEDOT:PF_6 fibers.[3]

Here we present the growth of PEDOT:PF_6 fibers by using AC electro polymerization. With the application of a biphasic signal between an electrode and a Pt-wire immersed in a monomer solution, dendritic fiber electrodes can be deposited on micro electrode arrays. In addition, by changing the parameters of the applied AC-signal, the growth and morphology of the dendritic fibers can be altered. Here we present the tunability by investigating the effects of the signal's voltage, frequency and applied time, on the morphology and electrochemical properties of the resulting electrodes.

Furthermore, we present the integration of dendritic fibers with primary neuronal cells. The neuronal interface was investigated through biocompatibility assays and electrophysiological recordings. The electrophysiological recordings, combined with scanning electron micrographs were used to characterize the cell-chip coupling between the fiber electrodes and the neuronal cells.

In summary, this novel PEDOT deposition technique allows the emulation of biological neuronal networks architectures. Therefore, dendritic fibers can be used in the future for a variety of applications to enhance the cell-chip coupling, thus bridging the gap between neuronal tissue and conventional electronic devices.

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Next-generation polymeric semiconductors for organic electrochemical transistors

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At this moment, we are still far away from understanding many neurologic diseases. However, the emergence of different bioelectronic technologies opens the pathway to fathom them once and for all. Organic electrochemical transistors (OECTs) can assist here, thanks to their superior recording of neurological signals. Moreover, their flexible nature allows application in non-invasive scalp electrode devices. Nevertheless, the field of OECTs is still in its infancy, and clear, rational design criteria are lacking. Hence, dedicated backbone and side-chain engineering could enlighten the structure-performance relationships for next-generation conjugated polymers that are able to transport both ions and electrons in future OECTs.

H2020 MITICS 964677

Single-molecule bioelectronic sensor: improving reliability with machine learning approaches

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Digitizing biomarkers analysis by quantifying them at the single-molecule level is the new frontier for advancing the science of precision health. The enhancement of the technical capabilities of bioelectronics systems, by giving clinicians the possibility to rely on biomarkers quantifications down to the single-molecule, holds the potential to revolutionize the way healthcare is provided. Such an analytical tool will indeed enable clinicians to associate a biomarker tiniest increase to the progression of a disease, particularly at its early stage.[1] Eventually, physicians will be able to identify the very moment in which the illness state begins. Such an occurrence will enormously enhance their ability to cure diseases by supporting better prognosis and permitting the application of precise treatment methods. The single molecule bio-electronic smart system array for clinical testing - SiMBiT - technology has been developed within the blooming field of precision medicine, leveraging on the single molecule with large transistor (SiMoT)[2] lab-based technology that can perform single-molecule detection of both proteins and DNA bio-markers.[3,4] Specifically, the SiMBiT technology has lately developed the SiMoT lab-based device into a cost-effective portable prototype multiplexing array that integrates, with a modular approach, standard components and interfaces with novel materials and exhibits enhanced sensing capabilities. The SiMBiT prototype has proven its potency in early detection of pancreatic cancer, being capable to discriminate among low-grade and high-grade mucinous cyst's lesions in peripheral biofluids, such as plasma samples. In this perspective, machine learning approaches play a pivotal role in developing classifiers for a fast, reliable multiparametric biosensors output.[5] Supervised model based on multivariate data processing has been undertaken to enable multiplexing, *i.e.* the simultaneous quantification of three biomarkers, namely MUC1 and CD55 proteins and KRAS DNA mutated sequence, in plasma and cysts' fluid samples. The main technological aspect of the SiMBiT device, with particular emphasis on the potency of machine-learning approaches, will be discussed.

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Aerosol Jet Printed Conductive Polymer Patterns for endothelial cell alignment inside a microfluidic chamber

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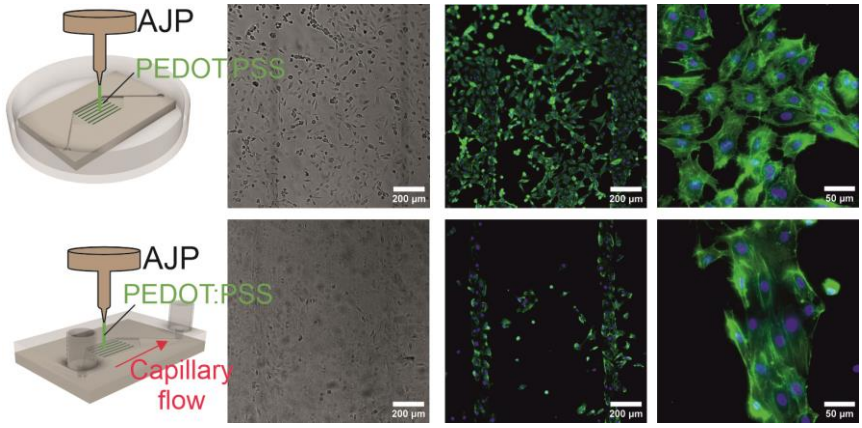
Endothelial cells (ECs) align with blood flow-induced shear stress (2 to 20 dyne cm^{-2}) to maintain vascular health[1]. Disrupted EC alignment indicates pathological conditions like atherosclerosis[2]. *In vitro*, aligned endothelium is crucial for studying vascular function. Microfluidic cultures expose ECs to shear stress to induce alignment, but uncontrolled stress can harm cells. Alternative methods include topographical and chemical substrate modifications[3]. Combining surface patterning and microfluidic culture is essential for proper EC alignment, minimizing the harmful effects of high shear stress while benefiting from its ability to reduce cell apoptosis.

Our work proposes the use of Aerosol Jet Printing (AJP), a contactless direct-writing technique, to precisely (resolution: 10 μm)[4] pattern PEDOT:PSS within a microfluidic PDMS chamber for Human Umbilical Vein Endothelial Cell (HUVEC) culture and alignment[5]. Conductive, biocompatible polymers, like PEDOT, promote ion exchange, enhancing cell proliferation and differentiation[6]. Unlike patterned extracellular matrix proteins, PEDOT:PSS patterns retained their chemical composition, molecular structure, transparency, and conductivity following oxygen plasma activation required for microfluidic PDMS device assembly ($\sigma = 340 \pm 126$ S cm^{-1} after plasma treatment). From 24 hours post-seeding, HUVECs cultured on PEDOT:PSS-patterned microfluidic chambers proliferated along the pattern under both static and capillary flow conditions. Notably, under capillary flow, cell proliferation occurred exclusively along PEDTO:PSS tracks up to the seventh day. For the first 3 days post-seeding, HUVECs' morphology mirrored the narrow pattern (6 parallel lines, W×L×H:50μm×8mm×100nm). Beyond this period, elongated and aligned morphology was maintained exclusively under capillary flow and cyclic shear stress along the same direction as the patterned lines.

Thus, the interplay of topographical constriction and capillary force-driven shear stress enabled EC reshaping without the need for external pumps. Additionally, the PEDOT coating, retaining electrical stability in a microfluidic device, can serve as a real-time cell monitoring sensor.



This figure visually summarizes how the PEDOT:PSS pattern and shear stress influence HUVECs' adhesion, alignment, and elongation under both static (top row) and capillary flow conditions within a micrometric PDMS chamber after one week of culture (fluorescent images show cell cytoskeleton in green and cell nuclei in blue).

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Azobenzene-substituted Poly-Thiophene Nanoparticles for the Photo-stimulation of Living Cells

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The use of biocompatible exogenous materials to allow the stimulation of living organisms avoiding genetic manipulation has been extensively proposed as an effective strategy. Poly-thiophenes have been employed for in vitro and in vivo photo-stimulation in the past years.[1,2] Polymer nanoparticles in close proximity to the cells can induce a perturbation in the membrane due to a charge displacement in the material, resulting in a physiological response.[3,4] Similarly, azobenzene-based molecules, able to insert in cells' membrane, can induce modifications in the membrane which can be reverted through photo-switching between trans- and cis-isomer.[5,6] At the same time, such photochromic molecules have also proved to be effective in interacting with bacteria.[7]
Here, we report the synthesis of a poly-thiophene with simple azobenzene substituents and the fabrication of nanoparticles. The proposed material, in the form of nanoparticles, shows a good affinity with living cells and can also induce a physiological response upon light excitation of the isomerization band. Such a system enables the simultaneous utilization of two different stimulation paradigms which may allow more precise targeting in the case of particularly functionalized azobenzene substituents. In fact, excitation bands of the thiophene and azobenzene substituents are spectrally separated. Tuning of the absorption and selectivity may be obtained with more specific azobenzene derivatives. Combination of the two different stimulation mechanisms may result in increased response when required.

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Conjugated Semiconducting Polymers For Geneless, Optically Driven Modulation Of Intracellular Redox Balance In Cardiovascular Cells

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In cell physiology, the term "redox homeostasis" refers to the balance between oxidizing and reducing agents and is recognized as a core concept governing the entire cell cycle. An imbalance in cellular redox status is intrinsically linked to the onset and progression of numerous diseases[1]. Specifically, Intracellular Reactive Oxygen Species (ROS) concentration plays a crucial role in the control and fine tuning of several physiological functions, from cell proliferation to differentiation, from migration to metabolic activity, to specific functionalities[2]. As a consequence, there has been a growing interest in the emerging field of 'redox medicine' over the past few years[3].

Currently available treatments to modulate the cell redox balance rely on the employment of chemically controlled methods. However, this strategy often fails to achieve accurate spatial and temporal control, is not reversible and is unsuitable for finely-tuned control of sub-cellular organelles. Employing optical excitation as a stimulus to precisely modulate intracellular ROS concentration at non- toxic levels offers the opportunity to overcome these limitations, but requires the development of novel, photoelectrochemically active transducers.

To support the development of new tools for precise, non-toxic, non-invasive and on-demand modulation of intracellular ROS concentration it is therefore necessary to develop new biocompatible materials, characterized by highly tunable electrochemical efficiency and good stability in a biological environment[4]. Moreover, stimulation protocols should be as minimally invasive as possible.

Here, we propose a novel strategy, based on the use of ad-hoc chemically functionalized semiconducting polymers, with enhanced opto-electrochemical properties[5,6]. We investigate the phototransduction process, highlighting how photoelectrochemical reactions occurring at the polymer/electrolyte interface can modulate ROS concentration on-demand.

We successfully employ extra- and intracellular delivery strategies, respectively based on polymer thin films and NPs, to achieve ROS increase within the *eu*stress dynamic range in relevant cardiovascular cell models. We demonstrate that photoelectrochemically active organic semiconductors developed in this work potentially satisfy all the requirements for innovative in-vivo redox-based therapies, potentially advancing clinical applications in the redox medicine field.

So, we investigate the possibility to exploit photo-activated ROS to activate redox-dependent biochemical pathways with pivotal roles in cardiovascular cells, such as calcium dynamics, nitric oxide modulation, angiogenesis process[8,9].

These results open up unexplored possibilities for wireless, geneless, and optically driven regenerative therapies in the cardiovascular domain, targeting the restoration of endothelial tissue functionality, the normalization of hypervascularization stages, and over a longer perspective the optical pacing of cardiac cells.

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Responsivity of the electrical double layer of metals/ or conducting polymers/ electrolytes interfaces to bias voltage and light

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The interface between conducting systems, namely metals and conducting polymers, and electrolytes plays a key role in various areas, such as organic electronics and devices for biological applications. We have recently reported on the modulation of the electrical double layer (EDL) potential by a tangential bias applied to the electronically conductive material (Figure 1). [1,2] More recently we have been investigating the effect of light exposure on the EDL potential.

Here, we report on these findings, discuss the possible explanations and implications on the processes occurring in several applications.

This work is supported by FCT-Portugal under the projects 2022.06045.PTDC and UIDB/50008/2020.

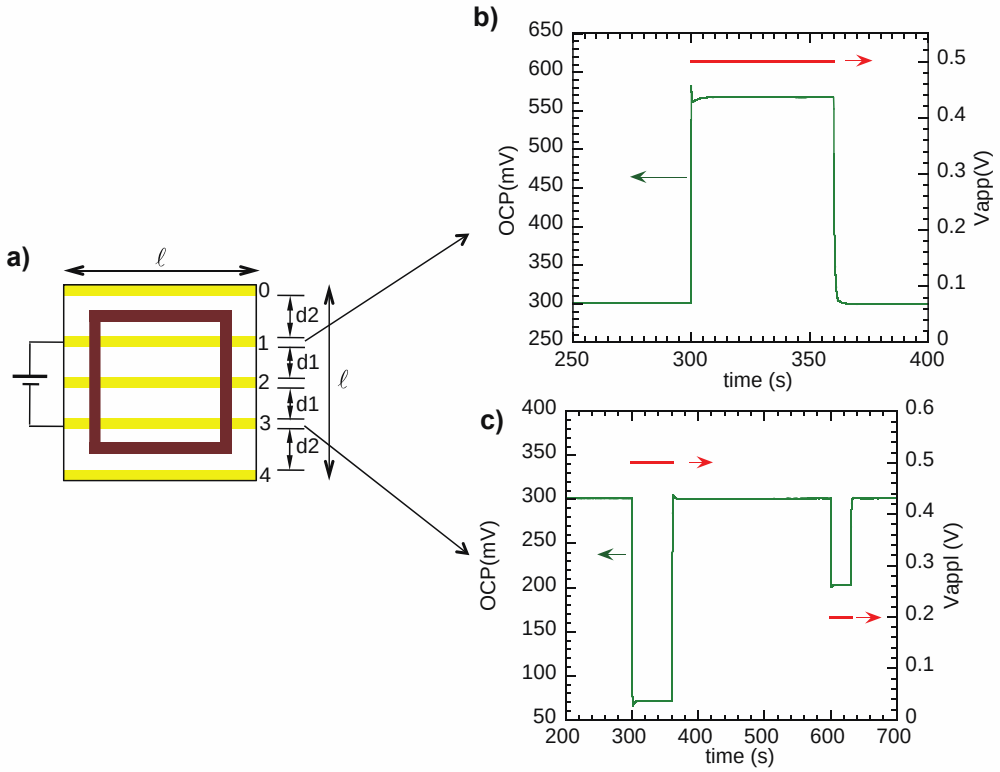

Figure 1. a) Structure of the setup, showing the ITO stripes under a PEDOT:PSS film that supports a container where the electrolyte (KCl, 0.1M, aq) is placed. b) Variation of the EDL potential at position 1 when a +0.5 V pulse (shown in red) is applied between contacts 1 and 3; c) Variation of the EDL potential at position 3 when a +0.5 V pulse followed by a +0.2 V pulse are applied between contacts 1 and 3. The decrease of the EDL potential under a bias of +0.2 V to 0.1 V evidences the scaling of the EDL potential change with the bias potential. Reproduced from Ref.1.

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Membrane-targeted push-pull azobenzenes for the optical modulation of membrane potential

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Optical technologies for non-genetic cell photostimulation are becoming increasingly influential in the biomedical field[1,2]. In this regard, Ziapin2, an amphiphilic alkyl-substituted 4,4'-diaminoazobene photoswitch, has been recently developed. Ziapin2 stably partitions into the cell membrane persisting in a trans configuration. The insertion in the membrane and the consequent formation of Ziapin2 dimers lead to a thinning of the membrane and an increase of the membrane capacitance. Light stimulation induces a *trans-to-cis* isomerization with a significant perturbation of the cell membrane potentials, able to trigger action potential firing in excitable cells without directly affecting the local temperature[3-5]. Since the increase in capacitance following the incorporation of Ziapin2 into the membrane leads to stable physiological changes in cells even in the absence of light, we propose a family of new membrane-targeted azobenzenes (MTs) with push-pull characteristics that can address these limitations. These molecules are fully water-soluble and naturally integrate into the cell membrane. Upon illumination, they undergo *trans-to-cis* isomerization, altering the local charge distribution and membrane potential modifications caused by light-driven alterations in the MT dipole moment within the cell membrane. Specifically, the photoisomerization of MTs results in distinct and reproducible depolarization followed by a slight hyperpolarization. The most promising compound, MTP2, has been extensively studied. Molecular dynamics (MD) simulations confirmed that MTP2 stably partition inside the cell plasma membrane without significantly affecting bilayer thickness. MTP2 was tested in a variety of cell types, including immortalized cell line (HEK293T cells), primary hippocampal neurons, and human induced pluripotent stem cells differentiated into cardiomyocytes (hiPSCs-CM), consistently demonstrating steady depolarization. Although not sufficient to trigger action potentials, the rapid light-induced depolarization shows potential applications, particularly in cardiac electrophysiology.

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Sensors of tomorrow: XTPL Delta Printing System & High Performance Materials

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Currently, there is an increase in the number of people suffering from chronic diseases, which is a global problem. Scientific progress in the area of broadly understood health technology will contribute to the digitization of health services in the coming years. Medical and genetic technologies, the Internet of Things, 3D printing, artificial intelligence and miniaturization of devices are just a few paths of solutions in this area [1]. Bioelectronics is currently an interdisciplinary science that strongly brings together scientists around the problems of reading the largest data platform, the human body, creating prospects for solutions with an incredible level of precision and personalization. By 2023, the biosensor market was estimated to be worth almost $30 billion. Moreover, this value is only expected to increase between 2024 and 2030 [2].

There are several challenges in this area, including achieving high accuracy in the detection of biological markers, developing small and easy to integrate or implant biosensors without compromising functionality, and maintaining constant performance over time in various biological and environmental conditions. Above all, the most important thing is to ensure safety during long-term contact with the biological tissues of the sensor. The idea of widespread use in medical care also requires meeting the requirement of high-quality biosensors with the possibility of scalability while maintaining an affordable price.

Following these needs, XTPL company introduced the pioneering technology of Ultra-Precise Deposition (UPD) to the market together with compatible metal high viscosity and highly concentrated, metal nanoparticles-based pastes. UPD system enables the deposit of various types of materials (pastes, ink or bio-compatible materials) and prints the desired structures with high conductivity in the microscale on rigid or flexible substrates, regardless of its planar or three-dimensional topography and surface energy, with high precision and resolution ranging from 0.5 to 100 micrometers. In this way, it is possible to perform 3D interconnections, edge interconnections, defect repair, microdots dispensing, and microvias filling (TSV, TGV, TCV) [3].

Nanopastes in the commercial offer, as well as those developed for specific applications, including biosensors, come with great control of various parameters such as: particle size and shape, size distribution, dispersion stability, surface tension, rheological properties, and adhesion ability to substrate. They are also compatible with other devices (e.g., precise dispensers and LIFT systems) and can therefore be used for the printing and deposition of functional micro features for medical devices.

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Biosensor Based on Carbon Nanotubes/Protein Hybrid Electrolyte Gated Transistors

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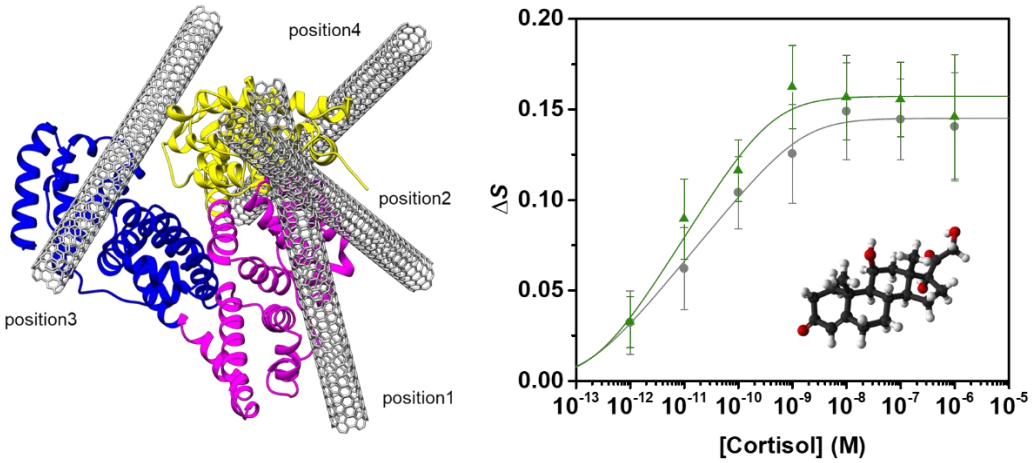
Semiconducting single walled carbon nanotubes (SWCNTs) are promising materials for biosensing applications with electrolyte-gated transistors (EGT).[1,2] However, their main drawback is their challenging solution processability for EGT fabrication, especially if compared with alternative, and widely exploited, active materials in organic electronics, such as small molecules (e.g., Pentacene) or polymers (particularly PEDOT:PSS and P3HT). Here, we introduce a simple water-based approach that allows fabricating EGT devices from stable dispersions of SWCNTs/bovine serum albumin (BSA) hybrids in solution.[3] The deposition of this dispersion onto a suitable substrate, allowed the formation of a random network of SWCNTs that serves as the semiconducting channel of the device. We demonstrate that this methodology allows the fabrication of EGT devices with electric performances that allow their use in biosensing applications. Hence, we exploit these devices for the detection of small molecules and proteins in solution, upon gate electrode functionalization with the appropriate antibodies. This is a robust and cost-effective methodology that sets the ground for a SWCNT/BSA-based biosensing platform that allows overcoming many limitations of standard SWCNTs biosensor fabrications.



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Light-responsive azo-tz-PEDOT:PSS electrode for cell interfacing

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In recent years, non-genetic optical methods have emerged as a promising approach for cell stimulation. These techniques utilize photoactive conductive substrates to trigger a response in cells through localized heating or electric charge generation, offering spatio-temporal resolution and avoiding the need for invasive voltages or genetic modification.[1] Organic p-type semiconductors, particularly the conductive polymer poly(3,4-ethylenedioxythiophene) polystyrene sulfonate (PEDOT:PSS), have gained substantial interest in the field. They offer biocompatibility, flexibility, stability, and dual electronic and ionic conduction, which are crucial for effective integration with biological environments.[2] Despite the progress made with pristine PEDOT:PSS, its application in optoelectronic cell stimulation is limited by low absorption in the UV-visible spectrum. There is a critical need for materials that combine excellent biocompatibility, stability and conductivity with great optical properties to enable efficient and controllable light-based cell stimulation.

This study aims to characterize a novel light-responsive derivative, azo-tz-PEDOT:PSS, which incorporates photoresponsive azobenzene moieties into a PEDOT:PSS film.[3] The goal is to evaluate its potential for organic optoelectronic cell interfacing by assessing the morphological, electrochemical and photoelectronic properties. The morphology of the films was analyzed using scanning electron microscopy (SEM), atomic force microscopy (AFM) and contact angle measurements. The electrochemical properties and stability of the material were examined through cyclic voltammetry and electrochemical impedance spectroscopy in both saline and cell media. Additionally, upon UV irradiation at 365 nm, the films generated photocurrent without the need for an external voltage bias, demonstrating effective charge injection dependent on the electrolyte composition and light intensity. Finally, biocompatibility tests using L-929 and retinal precursor R28 cell lines confirmed inconsiderable cytotoxicity.

The promising results suggest that azo-tz-PEDOT:PSS films can be further developed to exploit the spatio-temporal precision of light for more controlled cell stimulation. Future research will focus on exploring the effects of the photogenerated current on cellular activity. Additionally, modifications on the material could shift its absorption wavelength, increasing light penetration depth and enhancing biocompatibility.

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Engineering of Bacteria to See Light

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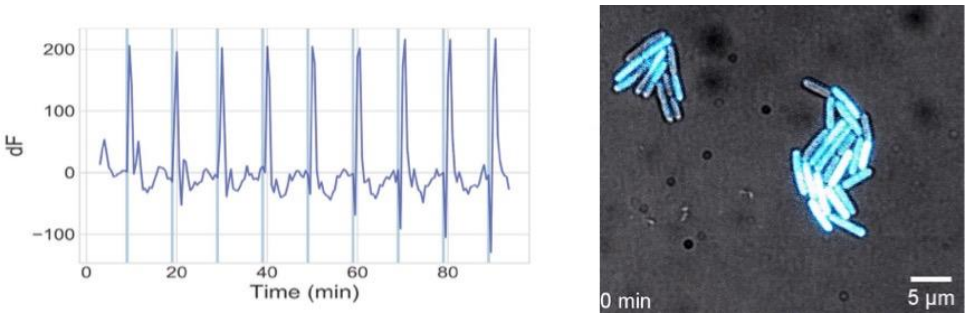
The possibility to control living matter with exogenous stimuli can have tremendous impact on synthetic biology, medicine and materials science, among others. For instance achieving control over cells behaviour remains a challenge at the interface between living and non-living matter,[1] and would enable the development of new bio-mimetic and bio-enabled materials able to perform tasks.[2] Within this context, bacteria have arisen as "active and actively-controllable materials", exhibiting neuro-like behaviour, extended bioelectric signalling[3,4] and tunable assembly properties.[5] In the last decade, it has been observed that the regulatory element of such an active behaviour is the electrical potential across the membrane, which governs bacteria electrophysiology, metabolisms and bioenergetics.[6] Light can be a powerful tool in these regards, as one can control the membrane potential and, thus, cell function and behaviour remotely and with relatively high spatiotemporal precision.

Here, I will show that membrane partioning of azobenzenes in bacteria can render these organisms responsive to light, without any genetic modification. In particular, we found that the isomerization reaction at the membrane location induces either hyperpolarisation or depolarisation of the potential depending on the excited state deactivation pathways, within a bio-mimetic mechanism reproducing the initial fate of retinal. I show that bacterial opto-stimulation can trigger neuron-like bioelectric signalling and can highlight the role of previously uncharacterized ion channels in bacteria electrophysiology.[7] Finally, I also show recent results on the light-modulation of antibiotic uptake, as well as perspectives on the photocontrol of bacterial motion and assembly behavior in consortia.



Periodic photo-induced hyperpolarization of a B. subtilis microcolony cultured with azobenzene and stimulated by 470nm light for 10 s every 10 min.

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Organic bio-mimetic electronics

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Bioelectronics is a rapidly advancing field of interdisciplinary research that merges biology and electronics.[1] Of particular interest to bioelectronics is related to biointerfaces, which refer to the interfaces or contact points where electronic devices interact with biological systems. It is desirable to design these interfaces in order to establish a seamless connection between the electronic components and the biological entities, enabling the efficient and multimodal exchange of information and signalng.[2,3] Poly(3,4ethylenedioxythiophene) doped with poly(styrene sulfonate) (PEDOT:PSS) is a promising and commercially available conductive polymer and is well-established in Organic Electrochemical Transistors (OECTs).[6]

At the biology side, cells are comprised by an external membrane which creates a complex network facilitating communication between external stimuli and internal components. Consequently, the development of an artificial membrane capable of mimicking its natural counterpart becomes crucial, serving as a versatile interface for bioelectronic devices.[4,5] One of the ways to accomplish that is by creating a Supported Lipid Bilayer (SLB), consisting of a thin lipid bilayer immobilized on a solid substrate, providing a stable and controlled environment for studying biological processes and interfacing with electronic devices, such as biosensors, neuromorphic and other bioelectronic devices.[5] The incorporation of SLBs in PEDOT:PSS films has been reported.[7] Nevertheless, the formation of multiresponsive SLBs in OECTs is still underexplored and will lead to creation of a biohybrid devices with great potential in bioemulation and biointerfacing.

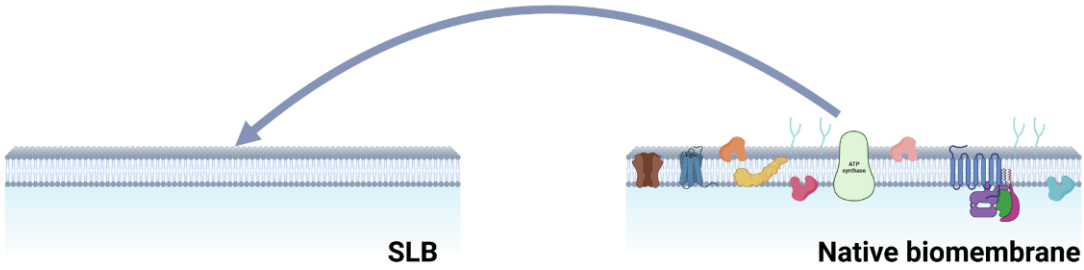

Figure 1. Schematic representation of how an artificial membrane can be synthesized (created with Biorender).

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Materials-Driven Strategies to Engineer Bacterial Motile Behaviour: Using Light to Understand and Control Dynamic Membrane Potential Modulation

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Understanding and controlling bacterial motility and response to external stimuli is indeed pivotal for leveraging bacteria in the creation of smart and living materials. Recent studies have unveiled the dynamic nature of bacterial membrane potential: it is now evident that membrane potential regulates a wide array of bacterial physiological processes and behaviors, including membrane transport, motility, antibiotic resistance, communication, and environmental sensing. Despite these advancements, numerous questions remain [1].

Traditional patch-clamp technique, while effective for certain applications, is inadequate for studying dynamic changes in bacterial membrane potential due to the requirement for cell immobilization and the diminutive size of bacterial cells. Consequently, there is an urgent need for developing novel, minimally invasive methods to measure membrane potential dynamics [2].

Fluorescent molecular probes with voltage-dependent optical properties have emerged as a promising solution for noninvasive studies of membrane voltage. In this context, Nernstian dyes have been widely employed due to their high efficiency and low toxicity. However, estimating membrane potential based solely on fluorescence intensity is fraught with challenges due to various factors such as spatial uniformity of excitation and fluctuations in light source power, which can lead to significant experimental errors. In contrast, fluorescence lifetime is an intrinsic property that depends solely on the local environment of the dye and is independent of many external experimental parameters. Thus, measuring both fluorescence intensity and lifetime can provide more accurate and reliable data.

In this study, we investigated the dependency of the fluorescence lifetime of the TMRM dye on the progressive depolarization of membrane potential in both gram-positive and gram-negative bacteria. Our findings demonstrate that this phenomenon is ubiquitous across different bacterial types, underscoring its potential as a robust tool for electrophysiological studies of motile and free-living bacteria in various environments. Furthermore, we employed Fluorescence Lifetime Imaging Microscopy (FLIM) to precisely correlate bacterial motility behavior with membrane potential modulation, using both intensity and lifetime as observables. These advancements enable the use of optical methods in bacterial electrophysiology, providing new insights into the dynamic processes of bacterial behavior and physiology. This approach could also be extended to study the detailed electrophysiology of other small motile cells, such as algae and viruses, which have not been extensively explored before but might serve as a new foundation for developing living materials.

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Investigating cellular responses of tissue-inspired hydrogels

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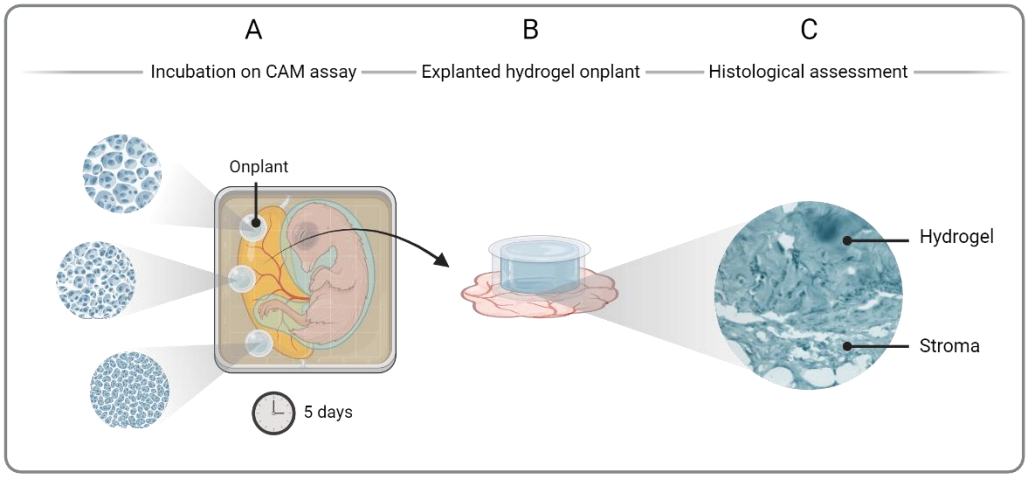
There is a growing trend in using soft, tissue-inspired materials for medical purposes. Our research examines interactions of biomimetic hydrogels with cells for tissue engineering, bioelectronics, and other biomedical applications. We used chorioallantoic membrane (CAM) assays to evaluate the attachment and integration of composite hydrogels made of two biocompatible materials, polyvinyl alcohol (PVA) and Phytagel (PHY). Three hydrogel recipes differing in their polymer proportions were incubated on the CAM for five days. Histological examination revealed significant cellular interactions at the hydrogel-CAM interface, varying with polymer concentration. We observed cell invasion into the hydrogel matrix, along with a remodeling of the chorionic epithelium and stroma, suggesting natural integration into host tissue. However, higher polymer density in the hydrogel was linked to adverse cellular reactions like a fibrotic response, indicating it may impair biocompatibility and integration. Human stem cells were cultivated on hydrogel substrates to better understand cellular and molecular interactions. Lactate dehydrogenase assays were conducted to prove that the materials used are not cytotoxic. These findings show that the hydrogel's structural and mechanical properties significantly impact bioadhesion and biointegration. Our results highlight the potential of tissue-inspired hydrogels to promote integration, tissue repair, and regeneration, emphasizing the need to adjust hydrogel composition to mimic host tissue.



(A) Illustration of three different hydrogel compositions placed on the CAM of a developing chick embryo. (B) Post-incubation, the explant with the CAM membrane and hydrogel onplant is excised for analysis. (C) Histological examination of the excised hydrogel-CAM interface shows cell invasion into the hydrogel and remodeling of the chorionic epithelium, indicating successful biointegration of the hydrogel into the host tissue.

Coupling organic neuromorphic devices with artificial and native neuronal membranes

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Advances in organic neuromorphic devices have paved the way for mimicking neuronal behaviour through flexible and biocompatible organic materials.[1,2] However, a major hurdle in neuroelectronics is reconciling the different mechanical and electrical properties of biological cells and electronic components.[3] To overcome this challenge, supported lipid bilayers (SLBs) coupled to organic neuromorphic devices have emerged as a compelling way to mimic the structure and composition of biological plasma membranes to support cell-chip interactions. Surface functionalization and modification of the surface charge of the bilayer can improve the electrostatic interaction between the artificial membrane and its biological counterpart and increase cell adhesion to SLBs.[4,5] Recent strategies also aim to induce other membrane surface phenomena such as blebbing to influence cell adhesion behaviour by changing the ratio of natural and artificial material in the mixture.[6,7]

This study introduces an innovative strategy to optimize SLB formation, encompassing both artificial and native neuronal membranes, onto conductive PEDOT:PSS and light responsive Azo/PEDOT:PSS polymers by vesicle fusion method. Size and surface charge of liposome and blebs were characterized by nanoparticle tracking analysis and dynamic light scattering. A thorough characterisation using various microscopy techniques such as confocal microscopy and atomic force microscopy as well as electrochemical techniques provides information about the resulting membranes. CV results confirmed SLB formation on both PEDOT:PSS and Azo/PEDOT:PSS by disappearing of characteristic peak currents of polymers as SLBs can block the electron transfer between the electrolyte and electrode. In agreement to CV results, EIS confirmed SLB formation on conductive polymers based on higher resistance and capacitance of SLB compared to substrates. In addition, membrane fluidity of SLB was studied by fluorescence recovery after photobleaching (FRAP). FRAP experiments were performed on both substrates to confirm SLB formation and monitor morphological changes in the Azo/PEDOT:PSS substrate by light irradiation in real time to generate "pop-up structures". This approach provides fully biomimetic and dynamic organic electrodes with a native neuronal membrane for biological recognition and offers a promising solution for developing neuromorphic devices and increasing the efficacy of neural interfaces.

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TAMM Plasmon for enhancement of the light-matter interaction

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Tamm Plasmon mode is a particular type of surface plasmon resonance excited by combining a distributed Bragg reflectors (DBR) and a plasmonic nanolayer made with a noble metal. Exploiting this electromagnetic mode, devices able to act as sensors, actuator and modulator can be manufactured. Starting from the achievements obtained by S. Normani et al. [1], a Tamm Plasmon Resonance device is produced by combining a metallic nanolayer, gold, and a Bragg crystal. Functionalizing the external face of the golden layer, the devise become capable to create specific interaction with precise species in the external environment. The device has been studied in combination with a photoactive polymer for the enhancement of the photo-driven phenomena of the latter.

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Bioelectronic Platform for Enhancing Plant Growth

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To cover the food demands of the growing population in the changing climate we need to increase crop yield in a sustainable manner. Hydroponics cultivation minimizes water and fertilizer use while it can be integrated in the urban environmen[1]. However, up until now the hydroponics substrates offer mainly mechanical support for the root system[2]. Here, we developed a bioelectronic platform that stimulates plant growth in hydroponics. We show that barley, one of the most important crops, grows well within the bioelectronic platform. When electrically stimulated, the dry weight of the barley seedlings increases by 50%, and the effect is evident in both root and shoot development during the growth period after the stimulation treatment. Results also show that stimulated plants reduce and assimilate NO_3^- more efficiently than controls, a finding that can have implications on minimizing fertilizers use. Our work may open the pathway for more sustainable practices in agriculture by bringing materials science-based solutions in hydroponics[3].

Figure 1. Stimulation of Barley seedlings resulting in enhanced plant growth. A) Schematic of plants growth and stimulation protocol where stimulation takes place between days 5 and day 10 and harvest on day 15 for *B*) Dry weight of the plant after 15 d of growth in eSoil with and without electrical stimulation.

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N-type electrolyte-gated organic transistors based on non-fullerene acceptor Y6

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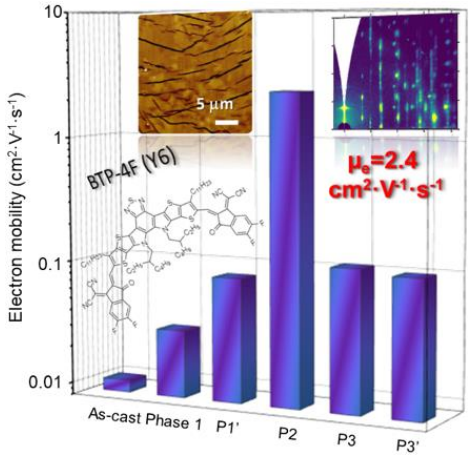
Electrolyte-gated organic transistors (EGOTs) are fundamental building blocks for the fabrication of electronic devices for near future bioelectronics applications. Indeed, these devices can be fabricated with solution processable bio-compatible materials that are well-suited to work in aqueous environments and physiologic media. Moreover, EGOTs are particularly attractive for bioelectronic applications due to their capability to transduce biological and biochemical inputs into amplified electronic signals.[1]

Although numerous EGOTs have been documented, the development of n-type devices, essential for creating complementary circuits, is scarce. In this work we employ the small molecule Y6, widely employed as non-fullerene acceptor (NFA) in bulk heterojunctions for photovoltaic applications, to fabricate n-type organic transistors. We show how Y6 exhibits excellent charge transport properties upon controlling its microstructure. Indeed, this NFA exhibits a rich polymorphism that we identified upon a thorough microstructural investigation, with a highly ordered polymorph, phase 2, exhibiting an electron mobility > 1 cm^2/Vs in standard organic field-effect transistors.[2] The integration of such highly crystalline and high mobility phase into an electrolyte-gated device leads to excellent n-type operational stability and illustrates the potentiality of non-fullerene acceptors in the realm of bioelectronics.



Charge carrier mobility of Y6 for different polymorphs.

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Electrolyte-Gated Organic Transistor with Hydrogel Gate for Monitoring Food Freshness

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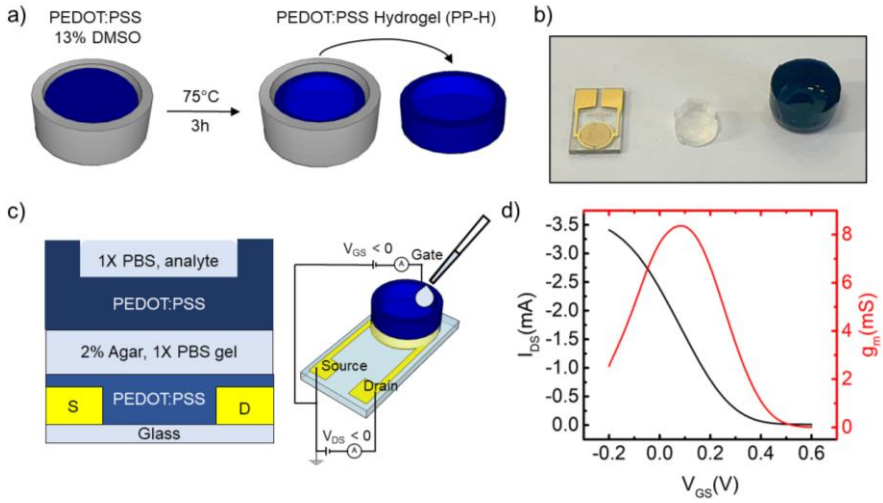
The Food and Agriculture Organization of the United Nations (FAO) reports that 14% of the world's food is lost annually between harvest and retail. It is urgent to reduce food waste from both ethical and economic perspectives. Implementing an efficient monitoring system for the cold chain, from the factory to the consumer, could be a crucial strategy to reduce food waste and simultaneously preserve consumer health. Sensors capable of quantifying the effective food freshness and quality could substantially reduce food waste and enable more effective food chain management.[1]

In the field of sensors, electrolyte-gated organic transistors (EGOT) based on organic semiconductors represent a promising technology, achieving outstanding performances in terms of limit of detection, signal amplification, sensitivity, and selectivity.[2]

We present a prototype of EGOT sensor for biogenic amines, generated by protein-rich food degradation. The device is based on a PEDOT:PSS hydrogel gate shaped like a beaker. This design allows us to pour the solution containing the target amines directly into the gate. Thanks to the weak bonds formed between the gate and the charged amines, we observe a concentration-dependent change of current in EGOTs with DPP-DTT and PEDOT:PSS channels.[3]

We demonstrate that the architecture enables the identification of two different amines (tyramine and ethylenediamine) within a concentration range from nM to mM, with a limit of detection of 100 pM for DPP-DTT devices.



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Polymer nanofibers for skeletal muscle cells alignment and photostimulation

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In tissue engineering, cell-substrate coupling has a crucial role. Its mechanical, chemical, physical and morphological features are decoded by cells as stimuli that strongly affect their behavior. [1] In muscular tissue engineering, in order to efficiently reproduce the natural muscle organization and achieve contraction ability, cell alignment on a suitably stiff substrate is required.[2] Here, electrospinning was used as technique to produce polymer nanofibers, used as scaffold for muscle cells. The polymers employed for these nanofibers must be biocompatible, for this purpose we selected polyvinyl alcohol (PVA). Preliminary study of substrate biocompatibility, cells alignment, cells differentiation and photostimulation were conducted on PVA nanofibers. Combing photochromic molecules and biocompatible polymers is it possible to obtain a blend photoactive material that can guide the cells growth and trigger the contraction of a muscle tissue at the same time. To promote muscle cells contraction electrodes are widely used; however, they may produce side effects like unnatural heating, Reactive Oxigen Spieces production.[3] Alternatively, photostimulation offers advantages such as better spatial and temporal resolution, low toxicity, and invasiveness.[4]
In these experiments we tested first PVA nanofibers with different orientation, suitability in promoting skeletal muscle cells differentiation. The next steps will involeve the synthesis of photoactive nanofibers through the crosslinking of photocromic molecules on the fibers surfaces. Before the fibers functionalization of the fibers, we characterized the optical properties of the molecules in different solvents, studying absorption properties, emission, and isomerization dynamics. Preliminary studies on the electrophysiology and viability of the photoactuator were conducted on HEK cells to better understand the effects of the molecules on the cells membrane.
The next steps will be to optimize the crosslinking process and verify the properties of the functionalized substrates first on HEK cells and then on muscle cells and to trigger a contraction through photostimulation.

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Multimodal Operando Probing of Mixed Conduction in Organic Electrochemical Transistors

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Organic Electrochemical Transistors (OECTs) have emerged as the most versatile building block for next-generation technologies ranging from biosensing to neuromorphic computing, including as a platform for fundamental studies and benchmarking mixed ionic-electronic conduction in materials. However, a precise unified understanding of voltage-dependent nano-to-mesoscale ionic and electronic charge transport occurring in operating OECTs under realistic conditions, concurrent with emerging structural and mechanical changes, is poorly understood, mainly due to the lack of multimodal and multiscale operando characterization techniques. Here, we addressed this challenge through automated[1] operando investigation of OECTs using in-liquid scanning dielectric microscopy[2,3] with multimodal functionality, which simultaneously tracks changes in relevant local electrical, mechanical, and morphological features as a function of applied bias voltages.[4] A one-to-one correlation between local changes and characteristic operating points in global device response across various operational regimes is established. By generalizing the device charging mechanism and considering interactions between different physical properties, we show that observed trends are an emergent behavior of OECTs, potentially directly affecting their operational and long-term stability. Our approach marks a foundational step towards unified multimodal experimental frameworks for unveiling intricate structure-property-function relationships in operating devices.

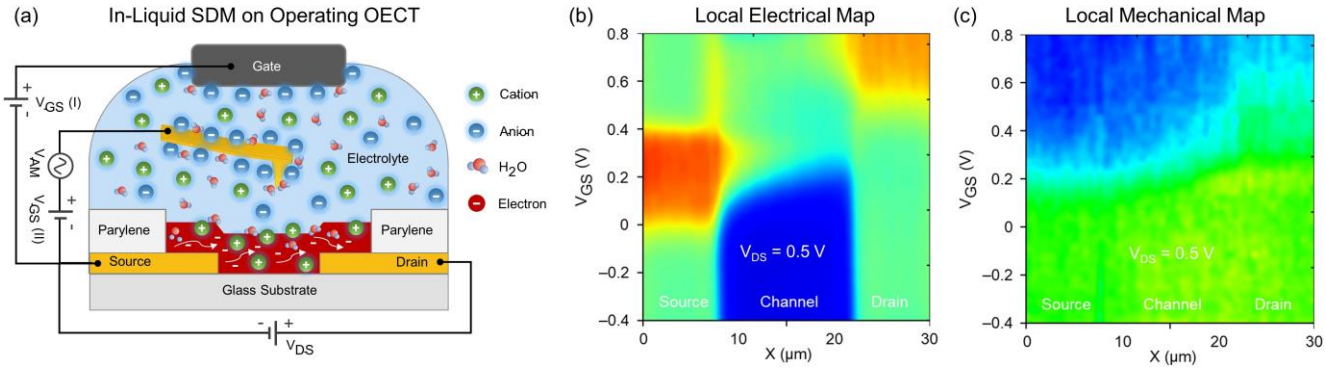

Figure: (a) Schematic of in-liquid SDM implementation on operating OECT, measuring local (b) Electrical and (c) Mechanical properties, besides morphology, as a function of bias voltages.

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Development of Neurohybrid Interfaces through electrodeposited PEDOT-Crown based Organic Electrochemical Transistors

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Neuromorphic devices, such as Organic Electrochemical Transistors (OECTs), have gained significant attention due to their unique properties like intrinsic ionic to electronic signal transduction, biocompatibility, and the ability to demonstrate short- and long-term plasticity, which make them an ideal candidate for interfacing and communicating with neurological systems.[1] In order to achieve a closer resemblance to the biological system and create innovative neuro-hybrid interfaces, new device and material concepts have been developed based on the emulation of the more intricate details of synaptic functioning. Recently, a novel material was introduced involving the modification of the semiconductive polymer Poly(3,4-ethylenedioxythiophene) (PEDOT) with crown ethers, combining the superior properties of PEDOT with the selective ion-sensing capabilities of crown ethers.[2] These new types of modified organic polymers have already demonstrated specific ion-dependent properties, but have yet to be investigated as the active channel material in OECTs.

This study focuses on the fabrication and characterization of PEDOT-Crown thin films, essential for their integration into neuro-hybrid interfaces. Comprehensive electrical and structural investigation of PEDOT-Crown was performed, exploring two different deposition techniques, such as cyclic voltammetry and chronoamperometry, to optimize film morphology and electrochemical properties. The films' performance was characterized across different electrolyte compositions to assess their electrolyte and ion-dependent properties.

A novel fabrication technique was demonstrated, achieving large-scale planar OECTs facilitating an electrodeposited PEDOT-Crown channel based on a PEDOT:PSS template, while analyzing their steady-state and transient responses in various electrolytes. This work demonstrates OECT operation using organic solvent-based electrolytes, revealing unique properties of PEDOT-Crown that are critical for future neuro-hybrid interfaces.

Future research will focus on gaining a deeper understanding of how crown ether modifications influence material properties. These advancements could pave the way towards tailored neuro-hybrid interfaces, leveraging the superior ion sensing and synaptic plasticity properties of PEDOT-Crown-based devices.

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Multifunctional and multi-layered opto-nanotransducers open new perspectives in the optical control of cell functions

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The control of biological functions is crucial for the in-depth understanding of physiological/pathogenic processes, as for the development of novel, ad hoc therapeutic modalities to fight specific diseases. In this regard, light-induced cell control is characterized by lower invasiveness, better space and time resolution, with respect to more traditional electrical-based methods. Exogenous inorganic and organic semiconducting materials have attracted considerable interest, since they can be employed as photoactive transducers to trigger the biological activity, without any need for viral transfection.[1] In particular, conjugated polymers offer great biocompatibility and stability together with geometrical adaptability. This class of materials was successfully employed for the modulation of the activity of different cell models, leading to several applications in medicine, including the modulation of neural growth, electrocardiography, artificial visual prosthesis and the modulation of angiogenesis.[2–6] The possibility to employ these materials in form of nanoparticles (NPs) offers multiple advantages for *in vivo* applications, like the possibility to employ variable routes of low invasive administration and to target specific sites, down to the subcellular length scale.[2,6]

In this scenario, photoelectrochemical phototransduction effects play a key role in the modulation of the physiological activity of cells. In particular, we showed that optically excited conjugated polymer NPs are able to reduce molecular oxygen, producing reactive oxygen species (ROS) at physiologically safe concentrations.[6] Low levels of ROS have been demonstrated to play a crucial role in cells, modulating several physiological processes. In this regard, several key-questions are currently open, and the in-depth characterization of the material/cell interface, as well as the optimization of conjugated polymer NPs phototransduction efficiency, are key aspects to be investigated.

Here, we fabricate composite, multi-layered NPs, composed by a conjugated polymer-based semiconducting shell and a conducting/semiconducting phase, acting as a dissociation interface, to boost the photoelectrochemical efficiency. We realize smart biointerfaces between the fabricated NPs and living cells. Firstly, we characterize the bio/polymer interface through a combination of transmission electron microscopy and confocal imaging. Secondly, we study the cell physiological properties by means of fluorescence microscopy and electrophysiology. We show that the combination of light excitation and NPs leads to the modulation of living cell physiology, in terms of electrical properties, intracellular ROS concentration, Ca^{2+} dynamics and cell redox balance. We demonstrate that the altered physiology affects several cellular processes, including proliferation and angiogenic response, depending on the material type and the characteristics of the light stimulus.

Overall, our results support the possibility to employ conjugated polymer-based NPs to regulate cellular functions, in a drug-free, touchless and spatio-temporally controlled manner, opening the way to several groundbreaking applications in medicine.

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Injectable Photovoltaic Microparticles for Photostimulation

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Light-induced production of reactive oxygen species (ROS) by nanoparticles has been discussed due to its high spatial and temporal resolution, non-invasiveness, and potential applications in diverse fields, including tissue regeneration. Light serves as a wireless power source, facilitating the transduction of energy into stimulation current, heat, or chemical reactions. The heat and/or chemical reactions can result in the generation of ROS, particularly hydrogen peroxide (H_2O_2), which offers the capability to open peroxide-sensitive ion channels, thereby triggering an action potential.[1,2]

Our research focuses on the light-induced redox reactions at the surface of photovoltaic particles, aiming to control H_2O_2 generation as previously studied with macroscopic devices.[3] Utilizing organic semiconductor materials, we have successfully established photovoltaic particles, even at thickness levels less than 100 nm. The photoactive layer absorbs light in a tissue transparency window (660 nm) enabling further *in vivo* applications. H_2O_2 production is achieved through an oxygen reduction reaction on the photoactive layer, with the concurrent oxidation of an electron donor on a conductive layer during continuous light exposure.

This study examines H_2O_2 production across various microparticle designs, considering the surrounding medium, from well-defined electrolytes with donors to complex cell culture media. We also investigate the effects of changing light source intensities, and duty cycles on the ROS generation process. Our findings show the potential of light-induced redox reactions on photovoltaic nanoparticles, with implications for a wide range of applications, particularly in the context of controlled tissue stimulation.

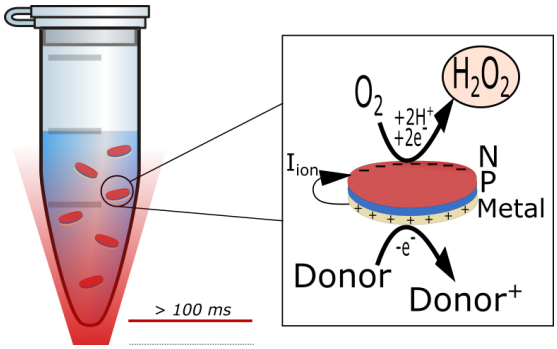

Figure 1: Light-induced redox reactions result in the production of H_2O_2 on the organic p-n junction layer with the simultaneous oxidation of a sacrificial donor

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Can organic semiconductors enable touchless control of cell mechanotransduction?

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Biophysical cues, especially mechanosensation, play a fundamental role throughout life, starting from early embryonic development over function and interplay of cells and tissues in the adult body up to regeneration processes. Tissue regeneration, which includes phenomena like cell division, differentiation, migration and expulsion is triggered by extracellular mechanical cues. Moreover, the body's capability to regenerate decreases with age, and therefore it impacts our life in sometimes detrimental aspects. Currently available tools to modulate or control mechanosensation often lack features necessary for in vitro and in vivo applications, in terms of efficiency, reliability, reversibility and spatial sensitivity.

Here, we show a novel approach to control mechanosensitive ion channels, through exogenous organic semiconductors. Materials in this class are fully biocompatible, thus offering the perspective for in vivo application, they can be easily processed in several forms, such as thin films, microstructured devices or nanoparticles. Most importantly, they are characterized by distinctive opto-electrical properties, providing excellent visible light responsiveness, as well as electronic and ionic conductivity.

In more detail, we preliminarily explore the opportunity to use organic semiconductors to control the activation of mechano-sensitive ion channels, in a reliable and effective manner. When shone with light, the materials demonstrate a collective movement, thus generating fully controllable shear stress stimulation. Our results may contribute to develop innovative smart materials for tissue regeneration driven by physical cues.

Photonic nanostructured interfaces for modulating keratinocyte activity

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The skin is the largest organ in the human body and consists of several layers, the outermost of which is the epidermis. Keratinocytes, the predominant cell type in the epidermis, are essential for maintaining skin integrity and barrier function. During wound healing, the dynamic process of proliferation, differentiation and apoptosis of keratinocytes, which are typically involved in the continuous renewal of the epidermis, is accelerated.[1]
These processes can be further modulated by nanostructured devices based on conjugated polymers and sensible to the green light to facilitate re-epithelialization of the wound site. Active interfaces with nanoscale components are particularly useful for interfacing and adapting to the complex nanoscale structural features of living tissues. Conjugated polymers are emerging as optimal candidates for interacting with living organisms due to their high biocompatibility and ability to combine the chemical and mechanical advantages of organic materials with the unique optoelectronic properties of semiconductors. Poly(3-hexylthiophene-2,5-diyl) (P3HT) is the chosen organic and photoelectrochemically active conjugated polymer. As a semiconductor, P3HT modulates the cell membrane potential through its interaction with cells, absorbing light in the visible spectrum and supporting charge photogeneration, which sustains both electronic and ionic charge transport.[2]
In this work we report the synthesis and optoelectronic and morphological characterization of biocompatible and photosensitive platform capable of modulating the epithelial cells physiology.
P3HT-based devices have the potential to open new frontiers in regenerative medicine, with significant implications for therapeutic strategies in the treatment of skin injuries and chronic wounds.

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Muscular cells non-genetic photostimulation and its robotics application

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The human-machine interface is generating a growing interest in finding application in robotic,[1] biological[2,3] and medical areas.[4] In particular, great interest is rising for the development of a contactless and wireless interaction. Within this context, light represents a clean and spatiotemporal precise tool to achieve such a goal.[5] Conjugated molecules and polymers offer a promising platform to interface with cells and living organisms due to their high optical absorption/emission cross section, chemical synthesis' easiness and relatively low toxicity.[6]

In this work, we present an optical method for stimulating the activity of muscular cells. The employed phototransducer is an amphiphilic azobenzene derivative named Ziapin2.[7,8] Here we started by the photostimulation mechanism, studied in a simple cell model.[9] Then we applied the Ziapin2-mediated stimulation to muscular cells (both cardimyocytes[10] and skeletal muscles cells[11]) reporting the effect on the signalling process in muscle cells at all the physiological levels of the contraction (electrophysiology, calcium transient and contraction). Finally we also tested this photostimulation approach on in vitro micro-physiological systems controlling its macroscopic contraction activity.[12]

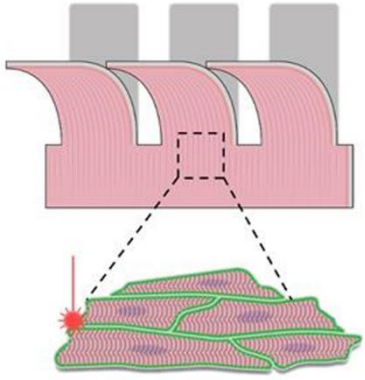

Figure 1 - Figure 1 – Sketch of a basic photostimulated bio-hybrid actuator.[12]

This last step consists of the realization of a bio-hybrid photoresponsive smart tissue, which is crucial for moving towards a real translational application and achieve the ultimate goal of this project. This can be a breakthrough for future applications in robotics and pharmacology, as well as tissue regeneration.

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Novel Conductive PEDOT:DBSA Hydrogel with Tunable Properties for Bioelectronics

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Pure conducting hydrogels seem to be very promising candidates for more efficient bioelectronics because of their high compatibility with tissues and mixed ionic-electronic conductivity. However, the preparatory processes of such hydrogels often require high temperature processes which excludes the presence of living cells during hydrogel preparation or injection of hydrogel precursors and gelation directly into tissues. Furthermore, most existing conductive hydrogels are based on PEDOT:PSS, whose biocompatibility was shown to be insufficient for some applications[1].
In this work, we report a preparation and characterization of conductive hydrogel based on a novel polymer composite PEDOT:DBSA, for cell stimulation in regenerative medicine. The preparatory process is facile and does not involve the use of non-conductive hydrogel templates. The hydrogel possesses excellent biocompatibility towards murine endothelial cells. The mechanical properties are tunable and in the range of soft biological tissues. The hydrogel shows low impedance at 1 Hz and mixed ionic-electronic conductivity, where the electronic one is one order of magnitude higher than the conductivity of biological tissues. Thus, this material holds the promise to form a truly functional interface between tissues and the bioelectronic device.

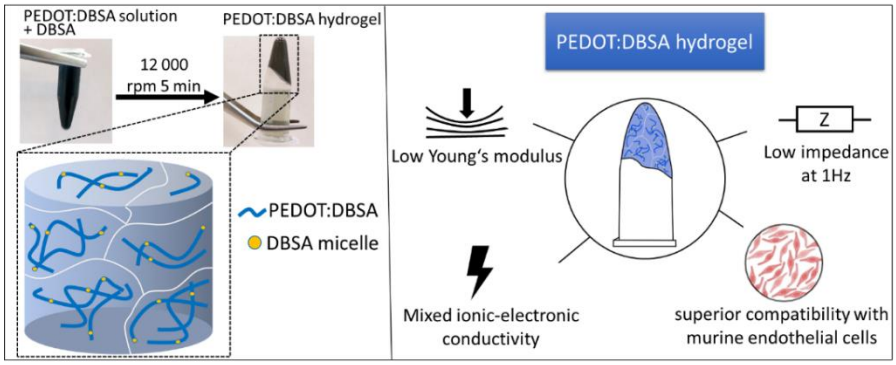

Figure 1: Summary of preparation and properties of pure conductive hydrogel based on novel PEDOT:DBSA.

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Specific sensing of perfluorinated pollutants (PFAS) in water with Electrolyte Gated Organic Transistors

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Pollution by Poly- and Perfluoroalkyl substances (PFAS) is a huge issue. These fluorinated organic compounds are widely used in industrial applications and their amphipathic nature due to the omniphobic carbon-fluorine chain and the hydrophilic head makes PFAS persistent pollutants which could easily spread and accumulate in water and soil all around the world.[1] In Europe more than 17˙000 sites are described as contaminated by PFASs. Moreover, PFAS are related to a long list of pathologic effects which includes liver diseases, brain diseases and endocrine system disorders.[2]
Liquid chromatography-tandem mass spectrometry is now the golden standard for PFAS detection, but it lacks scalability and portability for on-field and real time applications. Thus, the scientific community needs new techniques for fast and in-situ monitoring of PFAS pollution.
In this perspective, this work proposes an on-field deployable sensing platform based on the fluorophobic effect for PFAS detection. The sensor device is an Electrolyte Gated Organic Transistor (EGOT). The sensing capability is due to the gate electrode functionalized with a self-assembled monolayer (SAM) composed of a mixture of two thiols: one containing four-units oligo ethylene oxide (OEG) and the second presenting a perfluorinated chain, 1H,1H,2H,2H-Perfluorodecanethiol (PFDT). The organic semiconductive channel is made of a thin film of the polymer Poly[2,5-(2-octyldodecyl)-3,6-diketopyrrolopyrrole-alt-5,5-(2,5-di(thien-2-yl)thieno [3,2-b]thiophene)] (DPP-DTT) and distilled water is used as electrolyte.[3]
The EGOT sensor is used to detect and quantify different solutions containing increasing concentrations of Perfluorooctanoic acid (PFOA), Perfluorohexanoic acid (PFHxA), Perfluorobutanoic acid (PFBA), and Sodium Dodecyl Sulfonate (SDS) as non-specific control. A model to colleague the experimental data to the physics of the interaction between the PFAS and the EGOT is developed. And eventually we can affirm that the device exhibits a good specificity and a good selectivity, distinguishing PFAS of different lengths.
To integrate the device in an on-field deployable platform we also explore different architecture which could be interfaced with a microfluidic system.
This is the first example of a sensor based on an EGOT architecture for the detection of perfluorinated pollutants and it could help researchers in the development of a new class of sensors for the detection of PFAS in water and different substrates exploiting the fluorophobic effect.

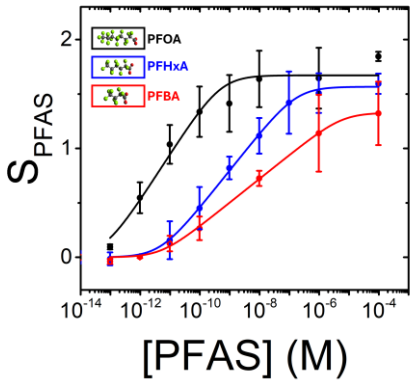

Figure 1: This figure represents the dose curves of the three different tested PFAS, signal (S_{PFAS}) vs PFAS concentration.

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Direct recording of action potentials of cardiomyocytes through solution processed planar electrolyte-gated field-effect transistors

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In the dynamic field of materials research, the drive for progress in cell-based biosensors remains crucial. These biosensors play a key role as *in-vitro* bioelectronic recording platforms of the electrical activity of electrogenic cells, such as neurons and cardiac cells.

Being able to achieve intracellular recordings of Action Potentials (APs) in a non-invasive way by using simple devices that can be easily fabricated and processed is fundamental in cardiology and neuroscience. The reason behind this relies on the information stored in the intracellular AP: its amplitude, shape and duration contain relevant information on the cell viability and health state which can be further used to study cardiac pathologies or to screen new drugs.

The available technologies able to achieve intracellular APs include invasive patch clamp technique, 3D nanostructures often combined with electro-/opto-poration methods and nanodevices such as nanowire field-effect transistors. However, these approaches mostly require complex manufacturing processes or are invasive in nature.

The aim of this work is therefore to propose a simple and cost-effective device that is able to record the electrical activity of *in-vitro* cell cultures in a spontaneous and non-detrimental manner.

To this end, we hereby demonstrate the direct recording of spontaneous intracellular action potentials of human induced pluripotent stem cells-derived cardiomyocytes (hiPSCs) by simple plating of cells on top of the channel of an Electrolyte-Gated Field Effect Transistor (EGFET).

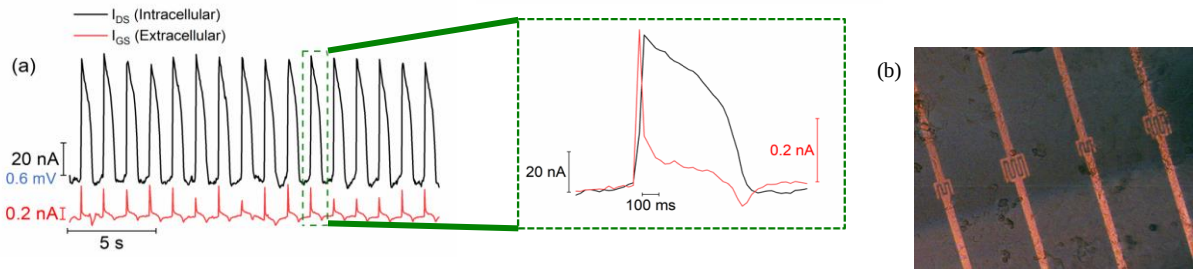
The EGFETs are based on solution-processed polymer-wrapped monochiral semiconducting single-walled carbon nanotubes (SWCNTs) which form a random interconnected network creating continuous charge transport paths from source to drain.

The APs of the cardiac cells were obtained by recording the transistor current at gate voltage V_{GS} corresponding to the maximum transconductance. The spontaneous APs of the cardiomyocytes change the effective gate voltage, that results in a modulation of the source-to-drain current I_{SD}.

The frequency of the modulated signal corresponds to the frequency of the beating cardiac cells. Shape and duration of the recorded signals confirms the fact that we were able to observe intracellular action potentials. The cell-coupling attained with our spin coated SWCNTs reveals very good signal strength and quality, while achieving high stability and reproducibility.

In addition, we demonstrate that the same planar EGFET can also be employed as a platform for electroporation with significant device performance and cell viability.

Ongoing innovations in cell recording technologies promise significant advancements and this platform can be used to unveil fundamental behaviors of cells and be further developed to become a future low-cost *in-vitro* tool.



a) Spontaneous recordings of the action potential of hiPSCs cardiomyocytes.
b) *Bright-field image of interdigitated EGFETs with cultured live hiPSC-CMs on top.*

A microfluidic platform to investigate the potential of Hydra vulgaris for biohybrid material fabrication

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The concept of using cell machinery to create hybrid materials in living tissues is a transformative idea in material science[1]. It aims to develop new materials made of living cells, displaying properties of both living and synthetic matter. The challenge of imbuing materials with living attributes is still significant in this field. In this fascinating field, we have recently demonstrated the capability of the small polyp Hydra vulgaris to act as a bioreactor, capable of fabricating conductive biofibers starting from thiophene based compounds.[2, 3] In our previous experiments, the organic semiconductor oligomer ETE-S (EDOT−thiophene−EDOT trimer) was observed to polymerize within Hydra's basal foot cells and secreted adhesive material, resulting in conductive structures[3].

In order to study and fully understand whether the conductive polymer structures affect the Hydra electrical behaviour, we have developed a multifunctional microfluidic platform, which allows, on the one hand, to control and adequately modify the physiological microenviroment of Hydra and, on the other hand, to investigate the modulation of electrophysiological activity, movements, and regenerative potential. Specifically, the microfluidic platform is fabricated using polydimethylsiloxane (PDMS), which is biocompatible, optically clear, simple to manufact, cheap and gas-permeable. An array of microchannels allows for the management of physiological microenviroment compositions as well as fluid flow. An integrated multi-electrodes array enables monitoring the electrophysiological activity of the Hydras in different parts of the body and in response to fluid changes. Finally, the system's transparency allows for optical and/or fluorescent imaging in order to correlate electrophysiological activity with morphological and biological activities as a function of induced variations in the physiological microenviroment. The obtained results lay the foundation to further employment of the animal cell machinery to assemble new biomaterials in vivo.

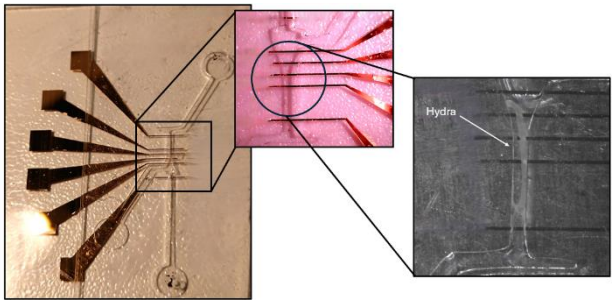

Figure 1. Multifunctional microfluidic platform used to stimulate and records electrical activity of Hydras.

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Inkjet-printed Electrode Arrays for extracellular recording and stimulation of electrogenic cells and tissues.

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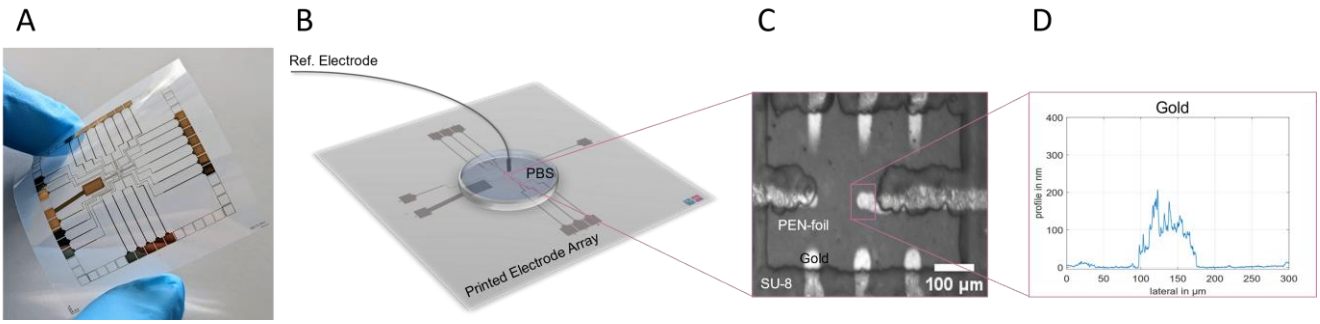
Electrode arrays are integral in connecting electronics with biological cells and tissues, a significant part of extracellular electrophysiology and neural implants. However, traditional microelectrode arrays are often rigid, potentially causing tissue damage.[1] Moreover, their fabrication requires costly and labor-intensive cleanroom techniques. Here, we introduce additively manufactured electrode arrays on flexible foils to address these challenges.

We have developed and characterized flexible gold electrodes fabricated using inkjet-printing. The electrodes were connected with silver nanoparticle ink feedlines and insulated with SU-8 (Figure (A), (C)). Comprehensive characterization was conducted using Dektak Profilometry, Atomic Force Microscopy, Impedance Spectroscopy, Cyclic Voltammetry, stability tests in cell culture, and stimulation tests (Figure B).

The electrodes demonstrated favorable surface roughness due to the additive printing process, contributing to a large effective surface area (see Figure (D)). Preliminary stability tests confirmed their stability in distilled water, phosphate-buffered saline (PBS), and cell culture environments for at least a week. Functional testing showed that the electrodes could stimulate tissues with a maximum current of approximately 6 µA for a 600 mV biphasic pulse applied to an electrode with a 48 µm diameter. The electrodes thus exhibited a charge injection capacity of about 2 µC/cm²/phase for a 600 mV stimulus.

The interfacing of an ex vivo mouse retina on the electrode array and successful electrophysiological recording confirmed the capability to measure extracellular membrane potentials. These results suggest that the inkjet-printed flexible gold electrodes are promising for applications in extracellular electrophysiology. In the future, we will investigate printing PEDOT:PSS on top of the gold electrodes to improve the electrochemical properties and stimulation capabilities of the electrode array.[2]



(A) Finished printed flexible electrode array. (B) Stimulation test setup with an Ag/AgCl reference electrode and a chamber filled with PBS. (C) Microscopy image of the printed electrodes for the stimulation tests. (D) Height profile of a printed gold track measured with a dektak profilometer.

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